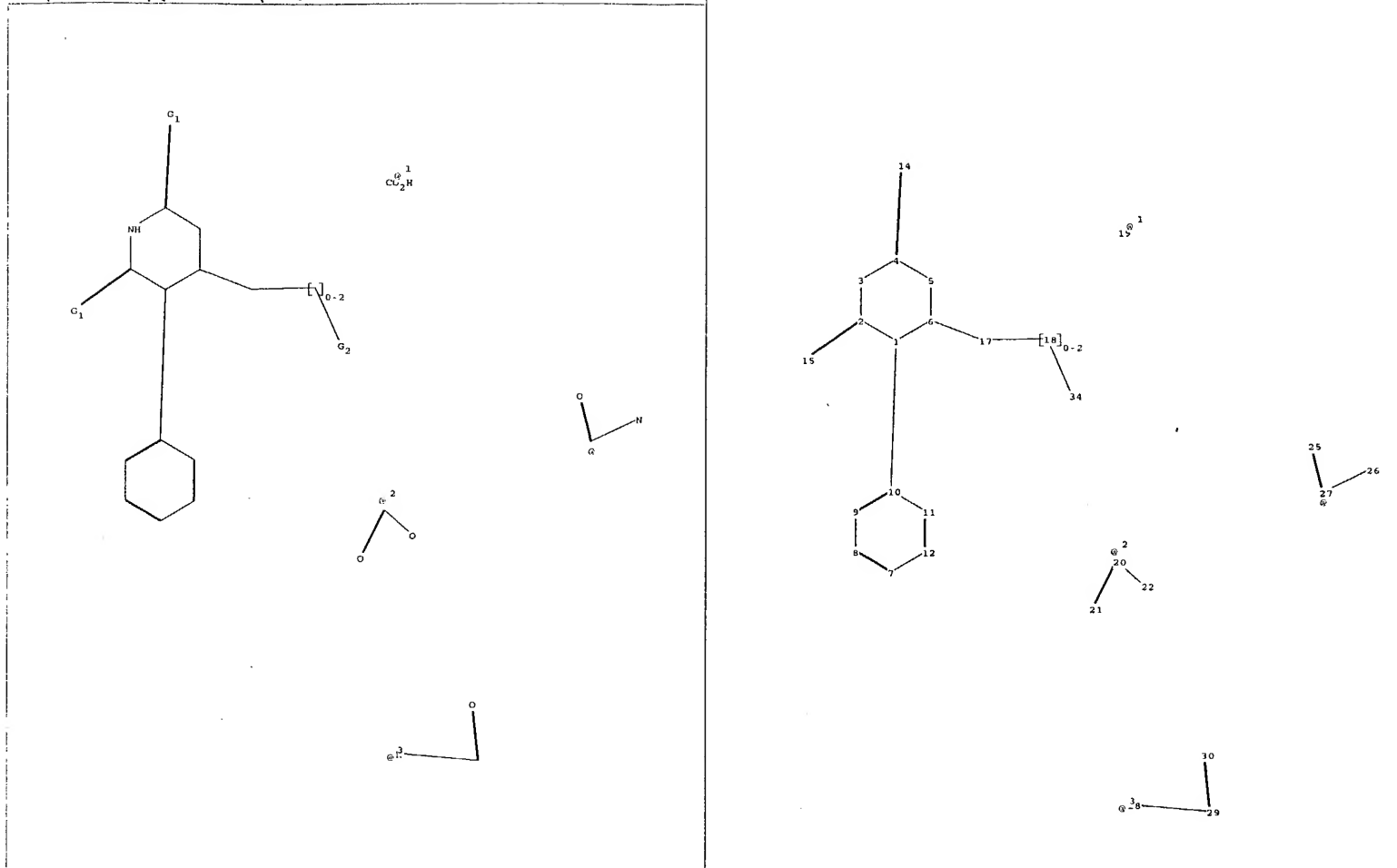


C:\stnweb\Queries\475a.str



chain nodes :  
 14 15 17 18 19 20 21 22 25 26 27 28 29 30 34  
 ring nodes :  
 1 2 3 4 5 6 7 8 9 10 11 12  
 chain bonds :  
 1-10 2-15 4-14 6-17 17-18 18-34 20-21 20-22 25-27 26-27 28-29 29-30  
 ring bonds :  
 1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12  
 exact/norm bonds :  
 1-2 1-6 2-3 2-15 3-4 4-5 4-14 5-6 18-34 20-21 20-22 25-27 26-27 28-29 29-30  
 exact bonds :  
 1-10 6-17 17-18  
 normalized bonds :  
 7-8 7-12 8-9 9-10 10-11 11-12  
 isolated ring systems :  
 containing 1 : 7 :

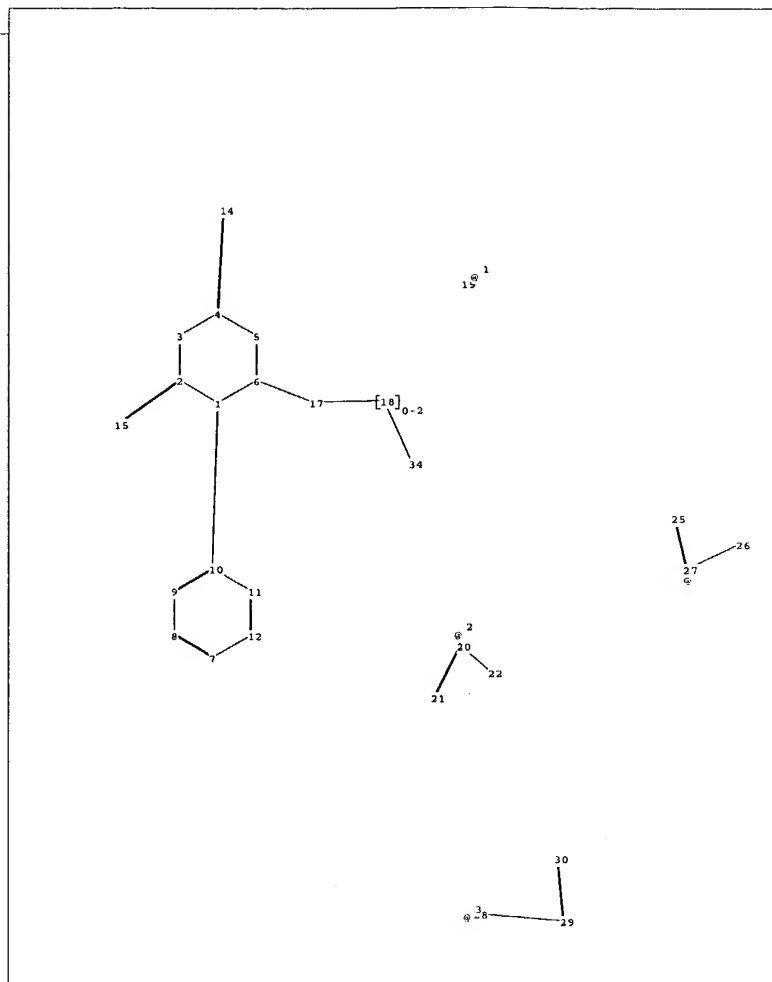
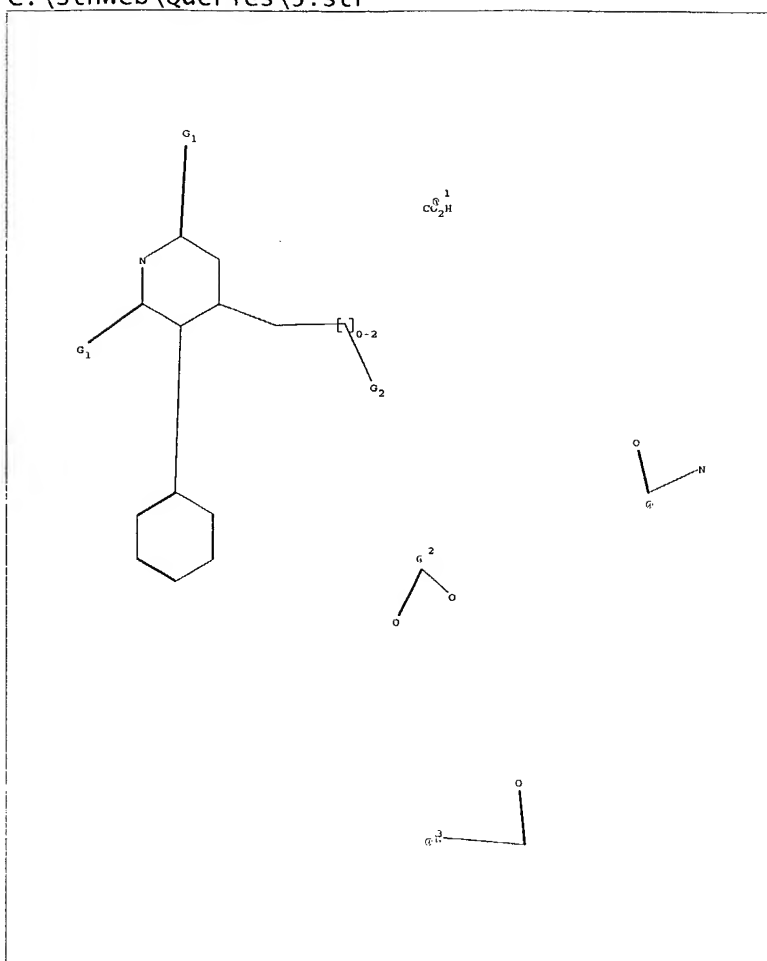
G1:O,S

G2:[\*1],[\*2],[\*3]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom  
 12:Atom 14:CLASS 15:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS  
 25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS 34:CLASS

C:\stnweb\Queries\3.str



```

chain nodes :
14 15 17 18 19 20 21 22 25 26 27 28 29 30 34
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12
chain bonds :
1-10 2-15 4-14 6-17 17-18 18-34 20-21 20-22 25-27 26-27 28-29 29-30
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 7-8 7-12 8-9 9-10 10-11 11-12
exact/norm bonds :
1-2 1-6 2-3 2-15 3-4 4-5 4-14 5-6 18-34 20-21 20-22 25-27 26-27 28-29 29-30
exact bonds :
1-10 6-17 17-18
normalized bonds :
7-8 7-12 8-9 9-10 10-11 11-12
isolated ring systems :
containing 1 : 7 :

```

G1:O,S

G2:[\*1],[\*2],[\*3]

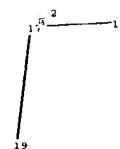
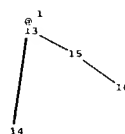
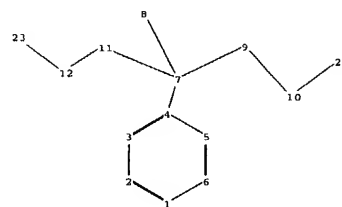
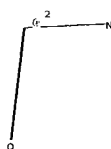
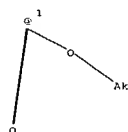
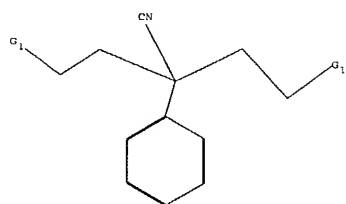
Match level :

```

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
12:Atom 14:CLASS 15:CLASS 17:CLASS 18:CLASS 19:CLASS 20:CLASS 21:CLASS 22:CLASS
25:CLASS 26:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS 34:CLASS

```

C:\stnweb\Queries\5.str



```

chain nodes :
  7  8  9 10 11 12 13 14 15 16 17 18 19 23 24
ring nodes :
  1  2  3  4  5  6
chain bonds :
  4-7  7-8  7-9  7-11  9-10 10-24 11-12 12-23 13-14 13-15 15-16 17-18 17-19
ring bonds :
  1-2 1-6 2-3 3-4 4-5 5-6
exact/norm bonds :
  10-24 12-23 13-14 13-15 15-16 17-18 17-19
exact bonds :
  4-7  7-8  7-9  7-11  9-10 11-12
normalized bonds :
  1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
  containing 1 :

```

G1:COOH,[\*1],[\*2]

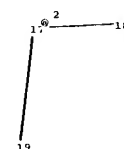
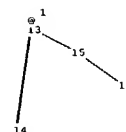
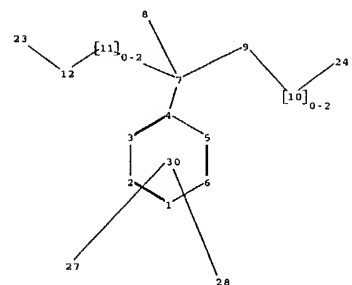
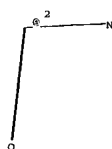
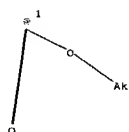
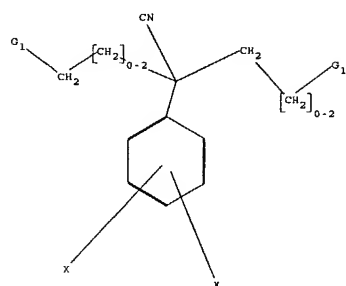
Match level :

```

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS
23:CLASS 24:CLASS

```

C:\stnweb\Queries\3k.str



chain nodes :

7 8 9 10 11 12 13 14 15 16 17 18 19 23 24 27 28

ring nodes :

1 2 3 4 5 6

chain bonds :

4-7 7-8 7-9 7-11 9-10 10-24 11-12 12-23 13-14 13-15 15-16 17-18 17-19

ring bonds :

1-2 1-6 2-3 3-4 4-5 5-6

exact/norm bonds :

10-24 12-23 13-14 13-15 15-16 17-18 17-19

exact bonds :

4-7 7-8 7-9 7-11 9-10 11-12

normalized bonds :

1-2 1-6 2-3 3-4 4-5 5-6

isolated ring systems :

containing 1 :

G1:COOH, [\*1], [\*2]

Match level :

1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:CLASS 10:CLASS  
11:CLASS 12:CLASS 13:CLASS 14:CLASS 15:CLASS 16:CLASS 17:CLASS 18:CLASS 19:CLASS  
23:CLASS 24:CLASS 27:CLASS 28:CLASS 29:CLASS 30:CLASS

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America  
 NEWS 2 "Ask CAS" for self-help around the clock  
 NEWS 3 JAN 27 Source of Registration (SR) information in REGISTRY updated  
 and searchable  
 NEWS 4 JAN 27 A new search aid, the Company Name Thesaurus, available in  
 CA/CAPLUS  
 NEWS 5 FEB 05 German (DE) application and patent publication number format  
 changes  
 NEWS 6 MAR 03 MEDLINE and LMedline reloaded  
 NEWS 7 MAR 03 MEDLINE file segment of TOXCENTER reloaded  
 NEWS 8 MAR 03 FRANCEPAT now available on STN  
 NEWS 9 MAR 29 Pharmaceutical Substances (PS) now available on STN  
 NEWS 10 MAR 29 WPIFV now available on STN  
 NEWS 11 MAR 29 New monthly current-awareness alert (SDI) frequency in RAPRA  
 NEWS 12 APR 26 PROMT: New display field available  
 NEWS 13 APR 26 IFIPAT/IFIUDB/IFICDB: New super search and display field  
 available  
 NEWS 14 APR 26 LITAlert now available on STN  
 NEWS 15 APR 27 NLDB: New search and display fields available  
 NEWS 16 May 10 PROUSDDR now available on STN  
 NEWS 17 May 19 PROUSDDR: One FREE connect hour, per account, in both May  
 and June 2004  
 NEWS 18 May 12 EXTEND option available in structure searching  
 NEWS 19 May 12 Polymer links for the POLYLINK command completed in REGISTRY

NEWS EXPRESS MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT  
 MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),  
 AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004

NEWS HOURS STN Operating Hours Plus Help Desk Availability  
 NEWS INTER General Internet Information  
 NEWS LOGIN Welcome Banner and News Items  
 NEWS PHONE Direct Dial and Telecommunication Network Access to STN  
 NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that  
 specific topic.

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 of commercial gateways or other similar uses is prohibited and may  
 result in loss of user privileges and other penalties.

\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 16:39:51 ON 16 MAY 2004

=> file reg

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file

provided by InfoChem.

STRUCTURE FILE UPDATES: 14 MAY 2004 HIGHEST RN 682152-60-9  
 DICTIONARY FILE UPDATES: 14 MAY 2004 HIGHEST RN 682152-60-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when  
 conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
 information enter HELP PROP at an arrow prompt in the file or refer  
 to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

L1 STRUCTURE UPLOADED

=> l1

L1 IS NOT A RECOGNIZED COMMAND

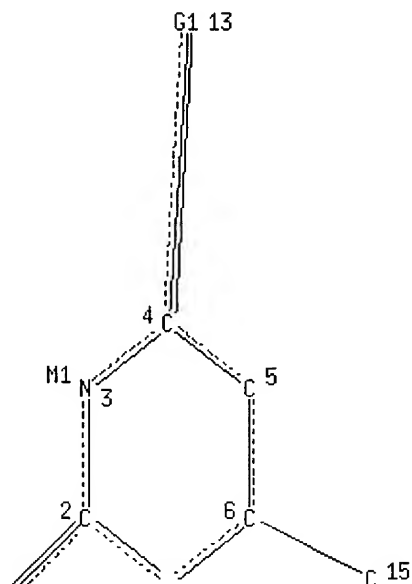
The previous command name entered was not recognized by the system.  
 For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

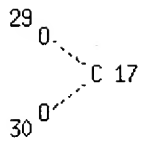
=> d l1

L1 HAS NO ANSWERS

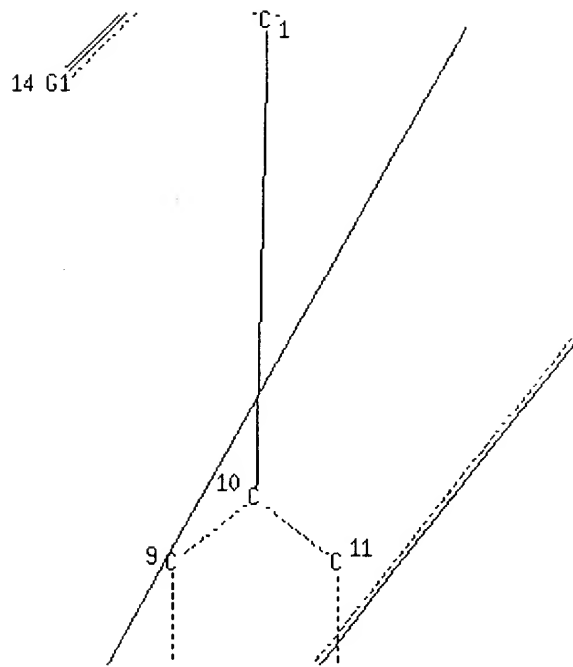
L1 STR

0 31 S 32

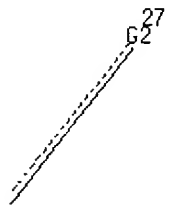




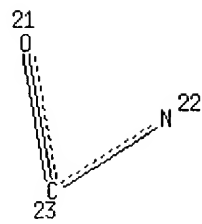
C 16  
Page 1-B

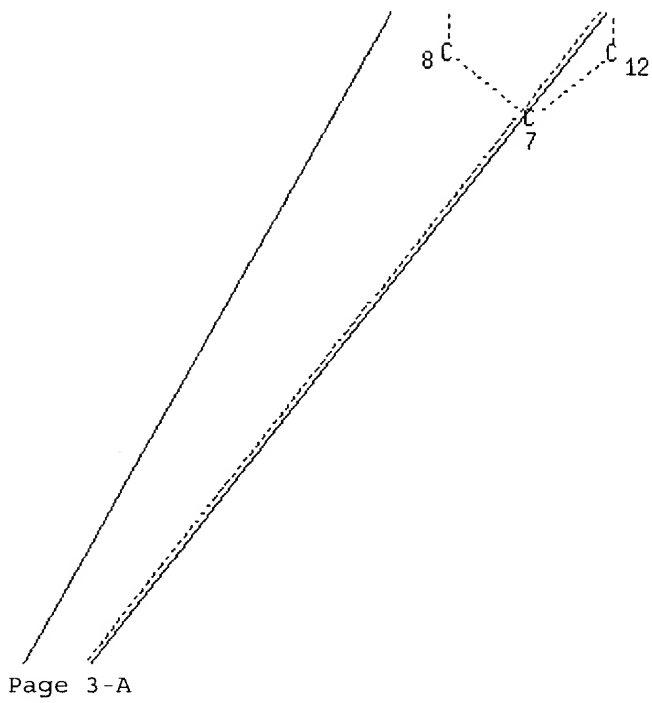


Page 2-A

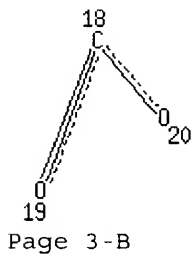


Page 2-B

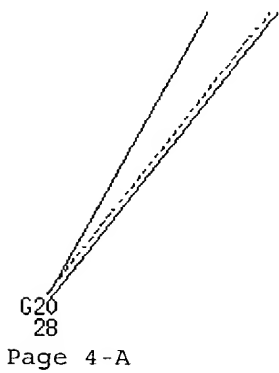




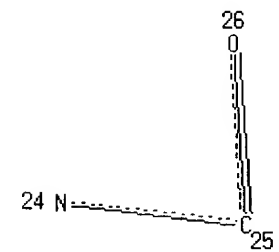
Page 3-A



Page 3-B



Page 4-A



Page 4-B

VAR G1=31/32  
VAR G2=17/18/24  
REP G20=(0-2) 16-15 16-27  
NODE ATTRIBUTES:



```

HCOUNT  IS M1      AT   3
NSPEC     IS R       AT   1
NSPEC     IS R       AT   2
NSPEC     IS R       AT   3
NSPEC     IS R       AT   4
NSPEC     IS R       AT   5
NSPEC     IS R       AT   6
NSPEC     IS R       AT   7
NSPEC     IS R       AT   8
NSPEC     IS R       AT   9
NSPEC     IS R       AT  10
NSPEC     IS R       AT  11
NSPEC     IS R       AT  12
NSPEC     IS C       AT  13
NSPEC     IS C       AT  14
NSPEC     IS C       AT  15
NSPEC     IS C       AT  16
NSPEC     IS C       AT  17
NSPEC     IS C       AT  18
NSPEC     IS C       AT  19
NSPEC     IS C       AT  20
NSPEC     IS C       AT  21
NSPEC     IS C       AT  22
NSPEC     IS C       AT  23
NSPEC     IS C       AT  24
NSPEC     IS C       AT  25
NSPEC     IS C       AT  26
NSPEC     IS C       AT  27
NSPEC     IS C       AT  28
NSPEC     IS C       AT  29
NSPEC     IS C       AT  30
DEFAULT MLEVEL IS ATOM
MLEVEL   IS CLASS AT  15 16 17 18 19 20 21 22 23 24 25 26 29 30 31 32
DEFAULT ECLEVEL IS LIMITED

```

## GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE

=&gt; s l1

SAMPLE SEARCH INITIATED 16:44:23 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

100.0% PROCESSED 4 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 4 TO 200

PROJECTED ANSWERS: 0 TO 0

L2 0 SEA SSS SAM L1

=&gt; s l1 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y

FULL SEARCH INITIATED 16:44:30 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 43 TO ITERATE

100.0% PROCESSED 43 ITERATIONS 0 ANSWERS  
SEARCH TIME: 00.00.01

L3 0 SEA SSS FUL L1

=> file beilstein

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

158.36

158.57

FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004

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FILE RELOADED ON OCTOBER 20, 2002

FILE LAST UPDATED ON MARCH 30, 2004

FILE COVERS 1771 TO 2003.

**FILE CONTAINS 8,932,479 SUBSTANCES**

>>> PLEASE NOTE: Reaction data and substance data are stored in  
separate documents and can not be searched together in one  
query.

Reaction data for BEILSTEIN compounds may be displayed  
immediately with the display codes PRE (preparations) and REA  
(reactions). A substance answer set retrieved after the search  
for a chemical name, a molecular formula or a structure search  
for example can be restricted to compounds with available  
reaction information by concatenation with PRE/FA, REA/FA or  
more general with RX/FA. The BEILSTEIN Registry Number (BRN)  
is the link between a BEILSTEIN compound and belonging reactions.  
For more detailed reaction searches BRNs can be selected from  
substance answer sets and searched in the next step as reaction  
partner BRNs - Reactant (RX.RBRN) or Product BRN (RX.PBRN).  
After a search for reaction details substance documents  
associated with reactants or products may be retrieved by  
searching RX.PBRNs or RX.RBRNs as BRNs. <<<

>>> FOR SEARCHING PREPARATIONS SEE HELP PRE <<<

\*\*\*\*\*  
\* PLEASE NOTE THAT THERE ARE NO FORMATS FREE OF COST. \*  
\* SET NOTICE FEATURE: THE COST ESTIMATES CALCULATED FOR SET NOTICE \*  
\* ARE BASED ON THE HIGHEST PRICE CATEGORY. THEREFORE; THESE \*  
\* ESTIMATES MAY NOT REFLECT THE ACTUAL COSTS. \*  
\* FOR PRICE INFORMATION SEE HELP COST \*  
\*\*\*\*\*

=>

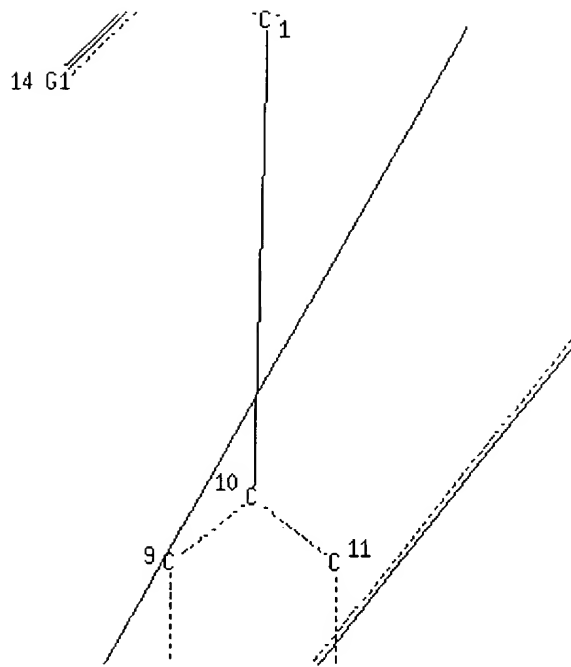
L4 STRUCTURE UPLOADED

=> d 14

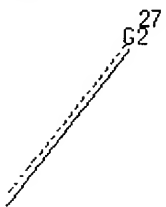
L4 HAS NO ANSWERS

L4 STR

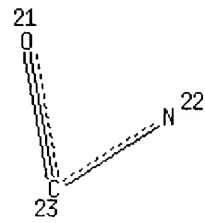


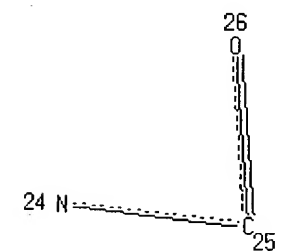
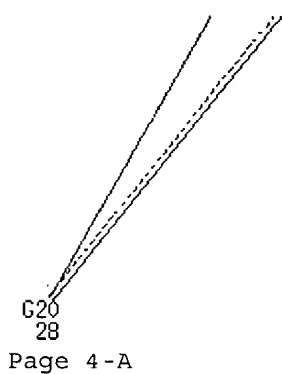
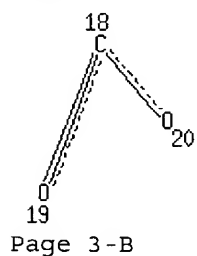
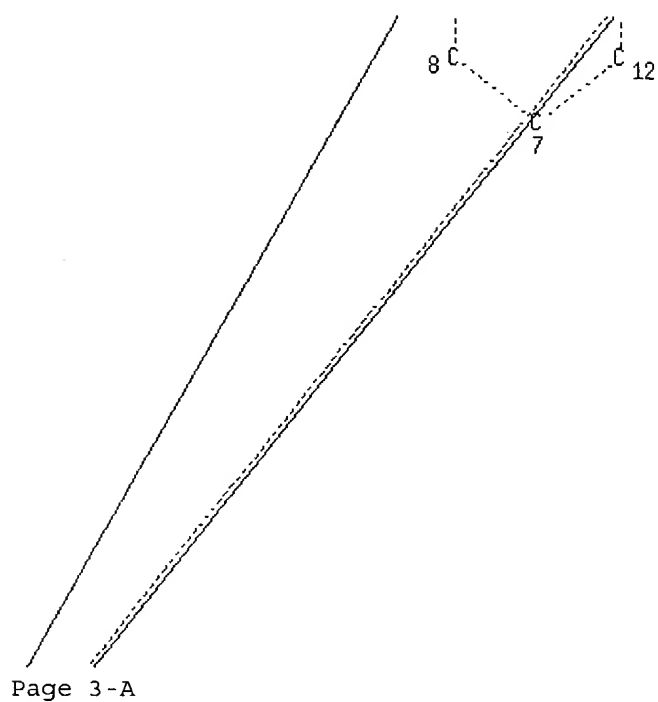


Page 2-A



Page 2-B





Page 4-B  
 VAR G1=31/32  
 VAR G2=17/18/24  
 REP G20=(0-2) 16-15 16-27  
 NODE ATTRIBUTES:

HCOUNT IS M1 AT 3  
 NSPEC IS R AT 1  
 NSPEC IS R AT 2  
 NSPEC IS R AT 3  
 NSPEC IS R AT 4  
 NSPEC IS R AT 5  
 NSPEC IS R AT 6  
 NSPEC IS R AT 7  
 NSPEC IS R AT 8  
 NSPEC IS R AT 9  
 NSPEC IS R AT 10  
 NSPEC IS R AT 11  
 NSPEC IS R AT 12  
 NSPEC IS C AT 13  
 NSPEC IS C AT 14  
 NSPEC IS C AT 15  
 NSPEC IS C AT 16  
 NSPEC IS C AT 17  
 NSPEC IS C AT 18  
 NSPEC IS C AT 19  
 NSPEC IS C AT 20  
 NSPEC IS C AT 21  
 NSPEC IS C AT 22  
 NSPEC IS C AT 23  
 NSPEC IS C AT 24  
 NSPEC IS C AT 25  
 NSPEC IS C AT 26  
 NSPEC IS C AT 27  
 NSPEC IS C AT 28  
 NSPEC IS C AT 29  
 NSPEC IS C AT 30

DEFAULT MLEVEL IS ATOM

MLEVEL IS CLASS AT 15 16 17 18 19 20 21 22 23 24 25 26 29 30 31 32

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE

=> s 14

SAMPLE SEARCH INITIATED 16:45:21 FILE 'BEILSTEIN'

SAMPLE SCREEN SEARCH COMPLETED - 0 TO ITERATE

100.0% PROCESSED 0 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.04

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
 BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 0 TO 0

PROJECTED ANSWERS: 0 TO 0

L5 0 SEA SSS SAM L4

=> file reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.12

158.69

FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004  
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.  
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 14 MAY 2004 HIGHEST RN 682152-60-9  
DICTIONARY FILE UPDATES: 14 MAY 2004 HIGHEST RN 682152-60-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
information enter HELP PROP at an arrow prompt in the file or refer  
to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=>

L6 STRUCTURE UPLOADED

=> 16

L6 IS NOT A RECOGNIZED COMMAND

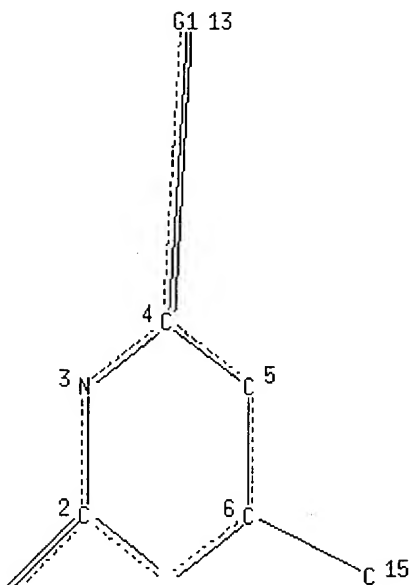
The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>):

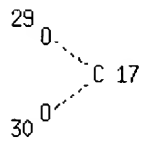
=> d 16

L6 HAS NO ANSWERS

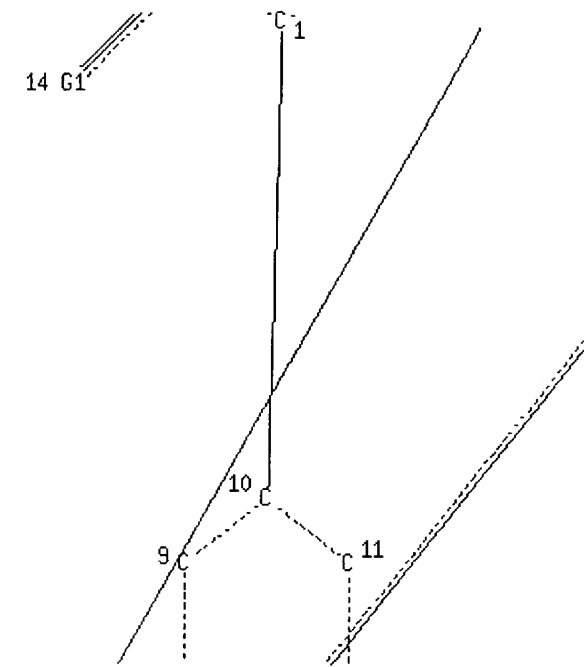
L6 STR

0 31 S 32

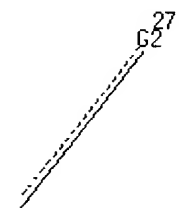




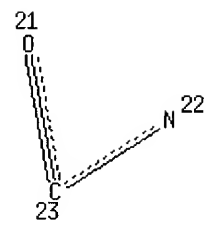
C 16  
Page 1-B



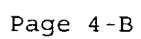
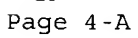
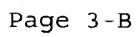
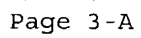
Page 2-A



Page 2-B







```
VAR G1=31/32
VAR G2=17/18/24
REP G20=(0-2) 16-15 16-27
NODE ATTRIBUTES:
```

```

NSPEC  IS R      AT   1
NSPEC  IS R      AT   2
NSPEC  IS R      AT   3
NSPEC  IS R      AT   4
NSPEC  IS R      AT   5
NSPEC  IS R      AT   6
NSPEC  IS R      AT   7
NSPEC  IS R      AT   8
NSPEC  IS R      AT   9
NSPEC  IS R      AT  10
NSPEC  IS R      AT  11
NSPEC  IS R      AT  12
NSPEC  IS C      AT  13
NSPEC  IS C      AT  14
NSPEC  IS C      AT  15
NSPEC  IS C      AT  16
NSPEC  IS C      AT  17
NSPEC  IS C      AT  18
NSPEC  IS C      AT  19
NSPEC  IS C      AT  20
NSPEC  IS C      AT  21
NSPEC  IS C      AT  22
NSPEC  IS C      AT  23
NSPEC  IS C      AT  24
NSPEC  IS C      AT  25
NSPEC  IS C      AT  26
NSPEC  IS C      AT  27
NSPEC  IS C      AT  28
NSPEC  IS C      AT  29
NSPEC  IS C      AT  30
DEFAULT MLEVEL IS ATOM
MLEVEL  IS CLASS AT  15 16 17 18 19 20 21 22 23 24 25 26 29 30 31 32
DEFAULT ECLEVEL IS LIMITED

```

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE

=> s 16

SAMPLE SEARCH INITIATED 16:46:25 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 4 TO ITERATE

100.0% PROCESSED 4 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS: 4 TO 200

PROJECTED ANSWERS: 0 TO 0

L7 0 SEA SSS SAM L6

=> s 16 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS

DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y

FULL SEARCH INITIATED 16:46:30 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 43 TO ITERATE

[illegible]

L8                      0 SEA SSS FUL L6

 $\Rightarrow \gamma$ 

L9            STRUCTURE UPLOADED

=> 19

L9 IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> s 19

SAMPLE SEARCH INITIATED 16:50:33 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 56 TO ITERATE

```
100.0% PROCESSED      56 ITERATIONS                      3 ANSWERS
SEARCH TIME: 00.00.01
```

```

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH    **COMPLETE**
PROJECTED ITERATIONS:   672 TO    1568
PROJECTED ANSWERS:      3 TO     163

```

L10                      3 SEA SSS SAM L9

=> § 19 full

```
THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:50:40 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 1412 TO ITERATE
```

```
100.0% PROCESSED      1412 ITERATIONS                      48 ANSWERS
SEARCH TIME: 00.00.01
```

L11 48 SEA SSS FUL L9

```
=> file hcaplus
```

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	313.36	472.05

FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004  
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FILE COVERS 1907 - 16 May 2004 VOL 140 ISS 21  
 FILE LAST UPDATED: 14 May 2004 (20040514/ED)

This file contains CAS Registry Numbers for easy and accurate  
 substance identification.

=> s l11

L12 69 L11

=> s l12 and castro, b?/au

342 CASTRO, B?/AU

L13 1 L12 AND CASTRO, B?/AU

=> d l13, ibib abs fhitrstr, 1

L13 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Citing  
 Text References

ACCESSION NUMBER: 2000:441776 HCAPLUS  
 DOCUMENT NUMBER: 133:73938  
 TITLE: Preparation of 3-(3,4-dihalophenyl)-2,6-dioxopiperidine-3-propionic acid alkyl esters as intermediates  
 INVENTOR(S): **Castro, Bertrand**; Dormoy, Jean-Robert; Rabion, Alain  
 PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.  
 SOURCE: PCT Int. Appl., 34 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037445	A1	20000629	WO 1999-FR2970	19991201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2787448	A1	20000623	FR 1998-16087	19981218
FR 2787448	B3	20010112		
EP 1140842	A1	20011010	EP 1999-973487	19991201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533327	T2	20021008	JP 2000-589517	19991201
US 6469173	B1	20021022	US 2001-857882	20010612
US 2003032810	A1	20030213	US 2002-175126	20020619
US 6686182	B2	20040203		

PRIORITY APPLN. INFO.:  
 FR 1998-16087 A 19981218  
 WO 1999-FR2970 W 19991201  
 US 2001-857882 A3 20010612

OTHER SOURCE(S): CASREACT 133:73938; MARPAT 133:73938  
 AB Title compds. and optically pure isomers were obtained either by

enantioselective enzymic hydrolysis of the racemic ester or by cyclisation of optically pure  $\text{HO}_2\text{CCH}_2\text{CH}_2\text{CR}(\text{CN})\text{CH}_2\text{CH}_2\text{CO}_2\text{R}_1$  ( $\text{R} = 3,4\text{-dihalophenyl}$ ,  $\text{R}_1 = \text{alkyl}$ ).

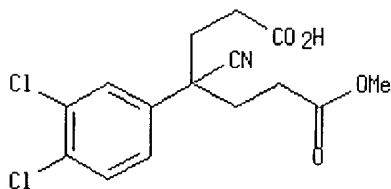
IT 279215-35-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of 3-(3,4-dihalophenyl)-2,6-dioxopiperidine-3-propionic acid alkyl esters as intermediates)

RN 279215-35-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, monomethyl ester, (-)-(9CI) (CA INDEX NAME)

Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 16:39:51 ON 16 MAY 2004)

FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004

L1 STRUCTURE UPLOADED  
L2 0 S L1  
L3 0 S L1 FULL

FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004

L4 STRUCTURE UPLOADED  
L5 0 S L4

FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004

L6 STRUCTURE UPLOADED  
L7 0 S L6  
L8 0 S L6 FULL  
L9 STRUCTURE UPLOADED  
L10 3 S L9  
L11 48 S L9 FULL

FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004

L12 69 S L11  
L13 1 S L12 AND CASTRO, B?/AU

=> s l12 not l13

L14 68 L12 NOT L13

=> s l14 and dormoy, j?/au

47 DORMOY, J?/AU  
L15 0 L14 AND DORMOY, J?/AU

=> s l14 and rabion, a?/au

27 RABION, A?/AU  
L16 0 L14 AND RABION, A?/AU

=> file reg

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	9.48	481.53
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-0.69	-0.69

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Property values tagged with IC are from the ZIC/VINITI data file  
 provided by InfoChem.

STRUCTURE FILE UPDATES: 14 MAY 2004 HIGHEST RN 682152-60-9  
 DICTIONARY FILE UPDATES: 14 MAY 2004 HIGHEST RN 682152-60-9

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2004

Please note that search-term pricing does apply when  
 conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more  
 information enter HELP PROP at an arrow prompt in the file or refer  
 to the file summary sheet on the web at:  
<http://www.cas.org/ONLINE/DBSS/registryss.html>

=> d his

(FILE 'HOME' ENTERED AT 16:39:51 ON 16 MAY 2004)

FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004

L1 STRUCTURE UPLOADED  
 L2 0 S L1  
 L3 0 S L1 FULL

FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004

L4 STRUCTURE UPLOADED  
 L5 0 S L4

FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004

L6 STRUCTURE UPLOADED  
 L7 0 S L6  
 L8 0 S L6 FULL  
 L9 STRUCTURE UPLOADED  
 L10 3 S L9  
 L11 48 S L9 FULL

FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004

L12 69 S L11  
 L13 1 S L12 AND CASTRO, B?/AU  
 L14 68 S L12 NOT L13  
 L15 0 S L14 AND DORMOY, J?/AU  
 L16 0 S L14 AND RABION, A?/AU

FILE 'REGISTRY' ENTERED AT 16:51:50 ON 16 MAY 2004

=> s l11/prep

'PREP' IS NOT A VALID CROSSOVER QUALIFIER FOR L11

Answer sets created in a different file may be field qualified with a limited set of qualifiers. Enter HELP CROSSOVER at an arrow prompt (=) for specific information.

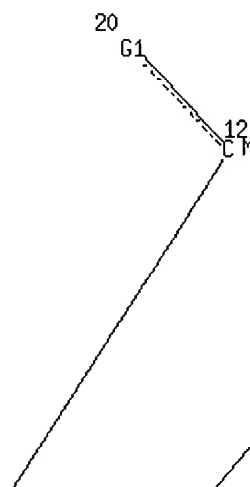
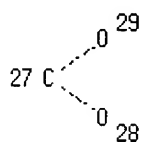
=>

L17 STRUCTURE UPLOADED

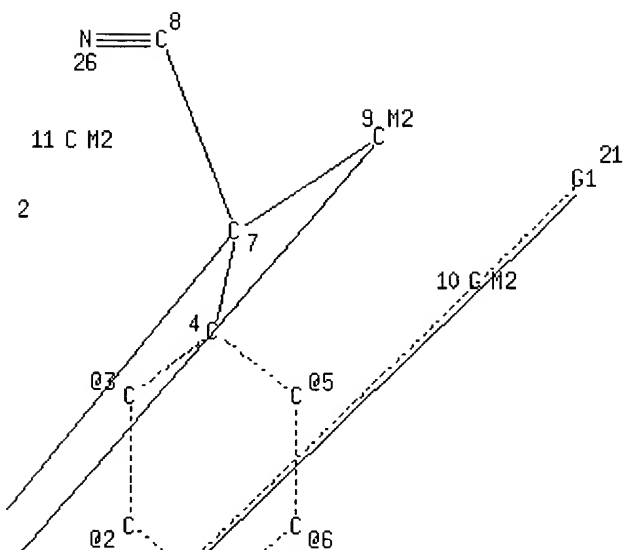
=> d l17

L17 HAS NO ANSWERS

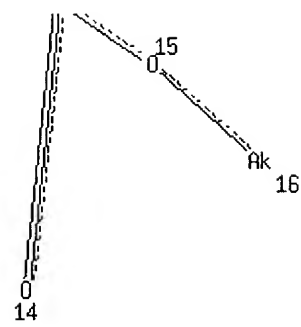
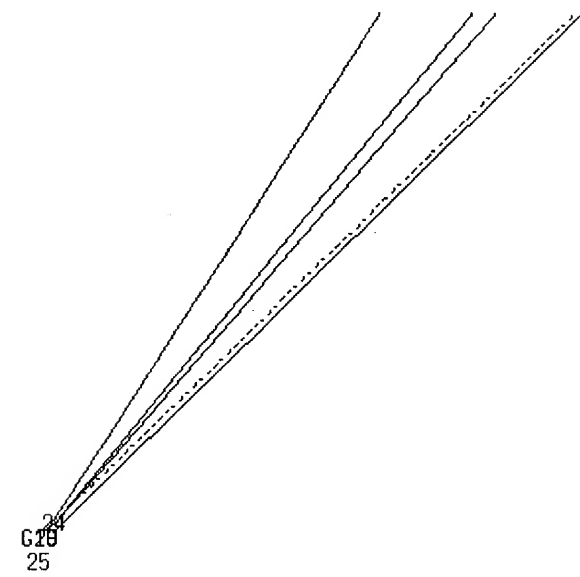
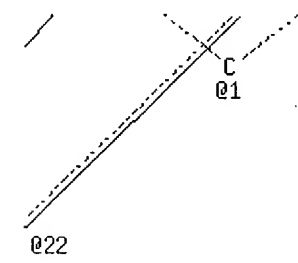
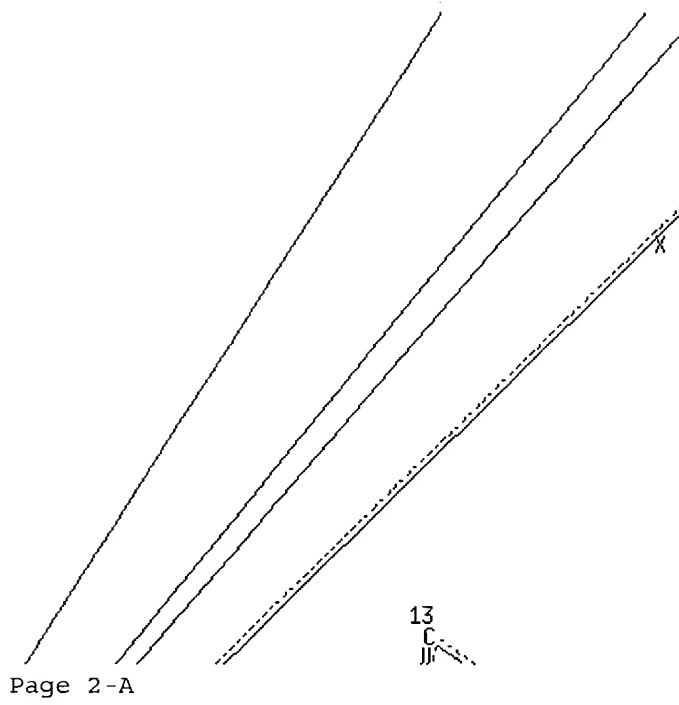
L17 STR



Page 1-A



Page 1-B





17 C-----N 18

0  
19

Page 3-B

VAR G1=27/13/17

REP G19=(0-2) 11-7 11-12

REP G20=(0-2) 10-9 10-21

VPA 22-1/2/3/5/6 S

VPA 23-1/2/3/5/6 S

NODE ATTRIBUTES:

HCOUNT	IS M2	AT	9
HCOUNT	IS M2	AT	10
HCOUNT	IS M2	AT	11
HCOUNT	IS M2	AT	12
NSPEC	IS R	AT	1
NSPEC	IS R	AT	2
NSPEC	IS R	AT	3
NSPEC	IS R	AT	4
NSPEC	IS R	AT	5
NSPEC	IS R	AT	6
NSPEC	IS C	AT	7
NSPEC	IS C	AT	8
NSPEC	IS C	AT	9
NSPEC	IS C	AT	10
NSPEC	IS C	AT	11
NSPEC	IS C	AT	12
NSPEC	IS C	AT	13
NSPEC	IS C	AT	14
NSPEC	IS C	AT	15
NSPEC	IS C	AT	16
NSPEC	IS C	AT	17
NSPEC	IS C	AT	18
NSPEC	IS C	AT	19
NSPEC	IS C	AT	20
NSPEC	IS C	AT	21
NSPEC	IS C	AT	22
NSPEC	IS C	AT	23
NSPEC	IS C	AT	24
NSPEC	IS C	AT	25
NSPEC	IS C	AT	26

DEFAULT MLEVEL IS ATOM

MLEVEL IS CLASS AT 7 8 9 10 11 12 13 14 15 16 17 18 19 22 23 26 27  
28 29

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 29

STEREO ATTRIBUTES: NONE

=> s 117

SAMPLE SEARCH INITIATED 16:54:34 FILE 'REGISTRY'  
SAMPLE SCREEN SEARCH COMPLETED - 164 TO ITERATE

100.0% PROCESSED 164 ITERATIONS 0 ANSWERS  
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*  
BATCH \*\*COMPLETE\*\*  
PROJECTED ITERATIONS: 2512 TO 4048  
PROJECTED ANSWERS: 0 TO 0

L18 0 SEA SSS SAM L17

=> s 117 full

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 155.00 U.S. DOLLARS  
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y  
FULL SEARCH INITIATED 16:54:38 FILE 'REGISTRY'  
FULL SCREEN SEARCH COMPLETED - 3193 TO ITERATE

100.0% PROCESSED 3193 ITERATIONS 9 ANSWERS  
SEARCH TIME: 00.00.01

L19 9 SEA SSS FUL L17

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	157.10	638.63
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-0.69

FILE 'HCAPLUS' ENTERED AT 16:54:42 ON 16 MAY 2004  
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FILE COVERS 1907 - 16 May 2004 VOL 140 ISS 21  
FILE LAST UPDATED: 14 May 2004 (20040514/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 119

L20                    26 L19

=> s 119/prep

26 L19

3147996 PREP/RL

L21                    26 L19/PREP

(L19 (L) PREP/RL)

=> s 120 and castro, b?/au

342 CASTRO, B?/AU

L22                    1 L20 AND CASTRO, B?/AU

=> d his

(FILE 'HOME' ENTERED AT 16:39:51 ON 16 MAY 2004)

FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004

L1                    STRUCTURE UPLOADED

L2                    0 S L1

L3                    0 S L1 FULL

FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004

L4                    STRUCTURE UPLOADED

L5                    0 S L4

FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004

L6                    STRUCTURE UPLOADED

L7                    0 S L6

L8                    0 S L6 FULL

L9                    STRUCTURE UPLOADED

L10                   3 S L9

L11                   48 S L9 FULL

FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004

L12                   69 S L11

L13                   1 S L12 AND CASTRO, B?/AU

L14                   68 S L12 NOT L13

L15                   0 S L14 AND DORMOY, J?/AU

L16                   0 S L14 AND RABION, A?/AU

FILE 'REGISTRY' ENTERED AT 16:51:50 ON 16 MAY 2004

L17                   STRUCTURE UPLOADED

L18                   0 S L17

L19                   9 S L17 FULL

FILE 'HCAPLUS' ENTERED AT 16:54:42 ON 16 MAY 2004

L20                   26 S L19

L21                   26 S L19/PREP

L22                   1 S L20 AND CASTRO, B?/AU

=> s 122 not 113

L23                   0 L22 NOT L13

=> d 122, ibib abs fhitrstr, 1

L22 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2004 ACS on STN

Full  
Text

Citing  
References

ACCESSION NUMBER:

2000:441776 HCAPLUS

DOCUMENT NUMBER: 133:73938  
 TITLE: Preparation of 3-(3,4-dihalophenyl)-2,6-dioxopiperidine-3-propionic acid alkyl esters as intermediates  
 INVENTOR(S): Castro, Bertrand; Dormoy, Jean-Robert; Rabion, Alain  
 PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.  
 SOURCE: PCT Int. Appl., 34 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000037445	A1	20000629	WO 1999-FR2970	19991201
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
FR 2787448	A1	20000623	FR 1998-16087	19981218
FR 2787448	B3	20010112		
EP 1140842	A1	20011010	EP 1999-973487	19991201
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002533327	T2	20021008	JP 2000-589517	19991201
US 6469173	B1	20021022	US 2001-857882	20010612
US 2003032810	A1	20030213	US 2002-175126	20020619
US 6686182	B2	20040203		

PRIORITY APPLN. INFO: FR 1998-16087 A 19981218  
 WO 1999-FR2970 W 19991201  
 US 2001-857882 A3 20010612

OTHER SOURCE(S): CASREACT 133:73938; MARPAT 133:73938

AB Title compds. and optically pure isomers were obtained either by enantioselective enzymic hydrolysis of the racemic ester or by cyclisation of optically pure HO<sub>2</sub>CCH<sub>2</sub>CH<sub>2</sub>CR(CN)CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>R<sub>1</sub> (R = 3,4-dihalophenyl, R<sub>1</sub> = alkyl).

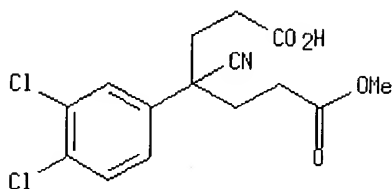
IT 279215-35-9P

RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. of 3-(3,4-dihalophenyl)-2,6-dioxopiperidine-3-propionic acid alkyl esters as intermediates)

RN 279215-35-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, monomethyl ester, (-)-(9CI) (CA INDEX NAME)

Rotation (-).



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d his

(FILE 'HOME' ENTERED AT 16:39:51 ON 16 MAY 2004)

FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004

L1 STRUCTURE UPLOADED  
L2 0 S L1  
L3 0 S L1 FULL

FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004

L4 STRUCTURE UPLOADED  
L5 0 S L4

FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004

L6 STRUCTURE UPLOADED  
L7 0 S L6  
L8 0 S L6 FULL  
L9 STRUCTURE UPLOADED  
L10 3 S L9  
L11 48 S L9 FULL

FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004

L12 69 S L11  
L13 1 S L12 AND CASTRO, B?/AU  
L14 68 S L12 NOT L13  
L15 0 S L14 AND DORMOY, J?/AU  
L16 0 S L14 AND RABION, A?/AU

FILE 'REGISTRY' ENTERED AT 16:51:50 ON 16 MAY 2004

L17 STRUCTURE UPLOADED  
L18 0 S L17  
L19 9 S L17 FULL

FILE 'HCAPLUS' ENTERED AT 16:54:42 ON 16 MAY 2004

L20 26 S L19  
L21 26 S L19/PREP  
L22 1 S L20 AND CASTRO, B?/AU  
L23 0 S L22 NOT L13

=> s l21 not l22

L24 25 L21 NOT L22

=> d l24, ibib abs fhitr, 1-25

L24 ANSWER 1 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

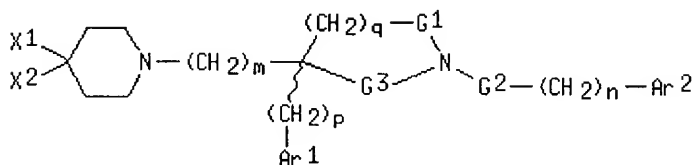
Full Citing  
Text References

ACCESSION NUMBER: 2001:896499 HCAPLUS  
DOCUMENT NUMBER: 136:20072  
TITLE: 1-Benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivatives and analogs as histamine and tachykinin receptor antagonists useful for the treatment of allergic diseases  
INVENTOR(S): Burkholder, Timothy P.; Bratton, Larry D.; Kudlacz, Elizabeth M.; Maynard, George P.; Kane, John M.;

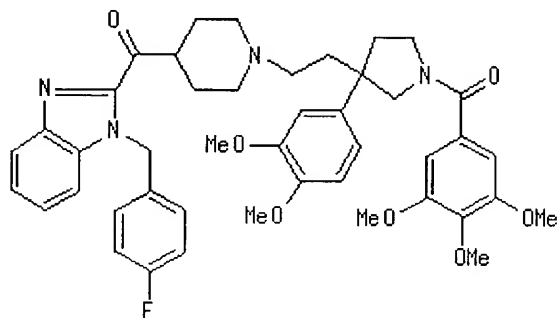
PATENT ASSIGNEE(S): Santiago, Braulio  
 SOURCE: Aventis Pharmaceuticals, Inc., USA  
 U.S., 77 pp., Cont.-in-part of U.S. Ser. No. 501,914,  
 abandoned.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6329392	B1	20011211	US 1998-79924	19980515
CA 2198084	AA	19960229	CA 1995-2198084	19950817
CN 1158612	A	19970903	CN 1995-195283	19950817
CN 1067385	B	20010620		
HU 76644	A2	19971028	HU 1997-1257	19950817
HU 221434	B	20021028		
AT 177095	E	19990315	AT 1995-931551	19950817
ES 2132709	T3	19990816	ES 1995-931551	19950817
ZA 9507033	A	19960416	ZA 1995-7033	19950822
IL 115040	A1	20000229	IL 1995-115040	19950823
TW 430663	B	20010421	TW 1995-84108797	19950823
PRIORITY APPLN. INFO.:			US 1994-295960	B2 19940825
			US 1995-501914	B2 19950713
OTHER SOURCE(S):		MARPAT 136:20072		

GI



I



II

AB The present invention relates to novel substituted piperidine derivs. I wherein: G1 is CH2 or CO; G2 is CH2 or CO; G3 is CH2 or CO; m is 2 or 3; n is 0 or 1; q is 1 or 2; p is 0 or 1; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl; Ar2 = (un)substituted Ph, pyridyl; X1 and X2 are defined in one of (A), (B), or (C): (A) X1 = H and X2 = substituted benzothiazole-2-carbonyl, diphenylmethyl, benzimidazolyl-2-carbonyl; (B) X1 = OH and X2 = substituted benzothiazol-2-yl, benzimidazol-2-yl; (C) X2 = (R5C6H4)C(Z1)(C6H4R6) wherein R5, R6 = from 1 to 3 substituents chosen independently from, e.g., H, halo, CF3, and X1 and Z1 taken together form a second bond between the carbon atoms bearing X1 and Z1; provided than

when G1 is CO, then G2 and G3 are CH<sub>2</sub>, and that when G2 is CO, then G1 and G3 are CH<sub>2</sub>, and that when G3 is CO, then G1 and G2 are CH<sub>2</sub>; stereoisomers thereof, and pharmaceutically acceptable salts thereof which are useful as histamine receptor antagonists and tachykinin receptor antagonists. Such antagonists are useful in the treatment of allergic diseases including: seasonal rhinitis, allergic rhinitis, and sinusitis. Thus, e.g., substitution reaction of 4-[1-(4-fluorobenzyl)-1H-benzimidazole-2-carbonyl]piperidine with 1-(3,4,5-trimethoxybenzoyl)-3-(3,4-dimethoxyphenyl)-3-(2-methanesulfonyloxyethyl)pyrrolidine (prepn. given) afforded II which exhibited H<sub>1</sub> receptor antagonism in vitro with pA<sub>2</sub> = 7.50, and NK<sub>1</sub> receptor binding affinity with IC<sub>50</sub> = 31 nM.

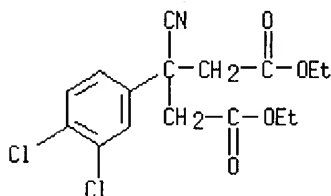
IT 40878-10-2P

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**  
(Preparation); RACT (Reactant or reagent)

(1-benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivs. and analogs as histamine and tachykinin receptor antagonists useful for treatment of allergic diseases)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



REFERENCE COUNT:

68

THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 2 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 2001:781460 HCAPLUS

DOCUMENT NUMBER: 135:344508

TITLE: Preparation of substituted  
benzimidazolyl[1,4]diazepanes useful as histamine and  
tachykinin receptor antagonists

INVENTOR(S): Maynard, George D.; Le, Tieu-binh

PATENT ASSIGNEE(S): George, Maynard,, USA

SOURCE: U.S. Pat. Appl. Publ., 122 pp., Cont.-in-part of U.S.  
6,194,406.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001034343	A1	20011025	US 2000-739741	20001218
US 6423704	B2	20020723		
US 6194406	B1	20010227	US 1997-513847	19971029
PRIORITY APPLN. INFO.:			US 1995-70907P	P 19951220
			US 1996-736411	B2 19961024
			US 1997-513847	A2 19971029

OTHER SOURCE(S): MARPAT 135:344508

GI

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB Title compds. I [m = 1 - 2; p = 0 - 1; G = CO, COCH<sub>2</sub>, SO<sub>2</sub>; R<sub>30</sub> = alkyl, vinyl, alkyl-oxy-alkyl-cyclopropyl, alkylheterocyclyl; R<sub>33</sub> = H, alkoxy, heterocyclyl, sulfonyloxy, etc.; R<sub>31-32</sub> = H, alkoxy] were prepd. Over 100 synthetic examples were provided. E.g., 3,4-dimethoxyacetoneitrile was alkylated twice with Et bromoacetate (THF, NaHMDS, dry-ice/acetone bath) and converted to 5-oxopyrrolidin-3-yl deriv. II (CoCl<sub>2</sub>•6H<sub>2</sub>O, MeOH, 20°C). II was converted to the pyrrolidine-alc. (THF, LAH, reflux, 18 h), N-acylated (CH<sub>2</sub>Cl<sub>2</sub>, NMM, 5°C, 3,4,5-(MeO)<sub>3</sub>C<sub>6</sub>H<sub>2</sub>COCl), converted to the mesylate (CH<sub>2</sub>Cl<sub>2</sub>, MsCl, Et<sub>3</sub>N, < 2°C - room temp. 18 h) and coupled to 4-(1-(2-ethoxyethyl)-1H-benzimidazol-2-yl)[1,4]diazepane (prepn. given, i-Pr<sub>2</sub>NEt, CH<sub>3</sub>CN, NaI, reflux, 3 days) to give example compd. III. I are histamine and tachykinin receptor antagonists (no data). Such antagonists are useful in the treatment of allergic rhinitis, inflammatory bowel diseases, Crohn's disease, ulcerative colitis, etc.

IT 40878-10-2P, 3-Cyano-3-(3,4-dichlorophenyl)pentanedioic acid diethyl ester

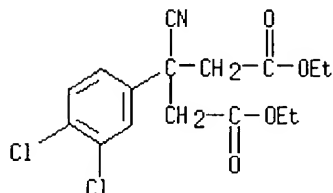
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**

(**Preparation**); RACT (Reactant or reagent)

(intermediate; prepn. of substituted benzimidazolyl[1,4]diazepanes useful as histamine and tachykinin receptor antagonists)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



L24 ANSWER 3 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER:

2001:240149 HCAPLUS

DOCUMENT NUMBER:

134:266309

TITLE:

Preparation of 4-(2-benzimidazolylamino)piperidines as histamine and tachykinin receptor antagonists

INVENTOR(S):

Kane, John M.; Maynard, George D.; Burkholder, Timothy P.; Bratton, Larry D.; Dalton, Christopher R.; Santiago, Braulio; Kudlacz, Elizabeth M.

PATENT ASSIGNEE(S):

Aventis Pharmaceuticals Inc., USA

SOURCE:

U.S., 106 pp., Cont.-in-part of U.S. Ser. No. 734,508, abandoned.

CODEN: USXXAM

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 5

PATENT INFORMATION:

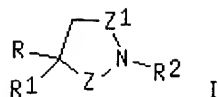
PATENT NO.

KIND DATE

APPLICATION NO. DATE



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 US 6211199 B1 20010403 US 1997-513846 19971215  
 PRIORITY APPLN. INFO.: US 1995-34609P P 19951117  
 US 1996-734508 B2 19961017  
 OTHER SOURCE(S): MARPAT 134:266309  
 GI



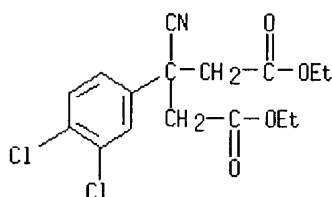
AB Title compds., e.g., I [R = R4Z4(CH2)m; R1 = (un)substituted Ph, -pyridinyl, -thienyl, etc.; R2 = (un)substituted (alkylenedioxy) benzyl, -benzoyl, etc.; R4 = e.g., (un)substituted 2-benzimidazolylamino; Z, Z1 = CH2 or CO; Z4 = piperidine-4,1-diyl; m = 2 or 3] were prepd. as histamine and tachykinin receptor antagonists (no data). Thus, 4-[1-(2-furylmethyl)-2-benzimidazolylamino]piperidine was condensed with 2-[1-[2-methoxy-5-(1-tetrazolyl)benzoyl]-3-phenyl-3-pyrrolidinyl]ethyl methanesulfonate (prepn each given) to give I [R = R4Z4CH2CH2, R1 = Ph, R2 = 2-methoxy-5-(1-tetrazolyl)benzoyl, R4 = 1-(2-furylmethyl)-2-benzimidazolylamino, Z = Z1 = CH2, Z4 = piperidine-4,1-diyl].

IT 40878-10-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (intermediate; prepn. of (benzimidazolylamino)piperidines as antiallergics)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
 (CA INDEX NAME)



REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

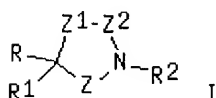
Full Text Citing References

ACCESSION NUMBER: 2001:149048 HCAPLUS  
 DOCUMENT NUMBER: 134:193454  
 TITLE: Preparation of N-(2-benzimidazolyl)-1,4-diazepanes as histamine and tachykinin receptor antagonists  
 INVENTOR(S): Kane, John M.; Maynard, George D.; Burkholder, Timothy P.; Bratton, Larry D.; Dalton, Christopher R.; Kudlacz, Elizabeth M.; Santiago, Braulio  
 PATENT ASSIGNEE(S): Aventis Pharmaceuticals Inc., USA  
 SOURCE: U.S., 108 pp., Cont.-in-part of U.S. Ser. No. 736,411.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6194406	B1	20010227	US 1997-513847	19971029
US 2001034343	A1	20011025	US 2000-739741	20001218
US 6423704	B2	20020723		

PRIORITY APPLN. INFO.:  
 US 1995-70907P P 19951220  
 US 1996-736411 B2 19961024  
 US 1997-513847 A2 19971029

OTHER SOURCE(S): MARPAT 134:193454  
 GI



AB Title compds. [I; R = R5Z5Z4(CH2)m; R1 = (CH2)rR4; R2 = Z3(CH2)nR3; R3 = (un)substituted Ph, -1,3-benzodioxol-5-yl, -1,4-benzodioxan-6-yl; R4 = (un)substituted Ph, -naphthyl, pyridinyl, -thienyl; R5 = H, (oxa)alkyl, (hetero)arylalkyl, etc.; Z, Z2 = CH2 or CO; Z1 = CH2 or CH2CH2; Z3 = CH2, CHMe, CO; Z4 = 1,4-diazepan-1,4-diyl; Z5 = (un)substituted benzimidazole-1,2-diyl; m = 2 or 3; n, r = 0 or 1] were prep'd. as histamine and tachykinin receptor antagonists (no data). Thus, e.g., I [R = 2-[4-[1-(2-ethoxyethyl)benzimidazol-2-yl][1,4]diazepan-1-yl]ethyl, R1 = 3,4-(MeO)2C6H3, R2 = COC6H2(OMe)3-3,4,5, Z = Z1 = Z2 = CH2] was prep'd.

IT 40878-10-2P

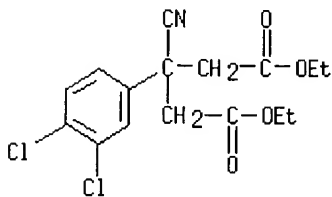
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**

(Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of benzimidazolyl diazepanes as antiallergics and antiinflammatories)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
 (CA INDEX NAME)



REFERENCE COUNT:

59

THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 5 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 1999:56370 HCAPLUS

DOCUMENT NUMBER: 130:124994

TITLE: Preparation of 4-aryl-1-[2-(1-benzoyl-3-pyrrolidinyl)ethyl]piperidine-4-carboxamides as NK1 and NK2 receptor antagonists

INVENTOR(S): Burkholder, Timothy P.; Maynard, George D.; Kudlacz, Elizabeth M.

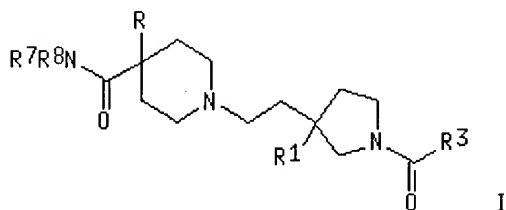
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA

SOURCE: U.S., 30 pp.  
 CODEN: USXXAM

DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5861417	A	19990119	US 1997-990672	19971215
PRIORITY APPLN. INFO.:			US 1997-990672	19971215
OTHER SOURCE(S):		MARPAT 130:124994		

GI



AB Title compds. [I; R = (un)substituted Ph or -pyridyl; R1 = (un)substituted Ph; R2 = ZR3; R3 = 1- or 5-tetrazolyl, 1,2,4-triazol-4-yl, etc.; R7,R8 = H; NR7R8 = piperidino, morpholino, (4-methyl)piperazino, pyrrolidino; Z = 6-(un)substituted-1,3-phenylene] were prepd. Thus, (S)-1-tert-butoxycarbonyl-3-(3,4-dichlorophenyl)-3-(2-mesyloxyethyl)pyrrolidine was aminated by 4-phenylpiperidine-4-carboxamide (prepn. each given) and the deprotected product amidated by 2-methoxy-5-(1-tetrazolyl)benzoic acid (prepn. given) to give (R)-I [R = Ph, R1 = C6H3Cl2-3,4, R2 = 2-methoxy-5-(1-tetrazolyl)phenyl, R7 = R8 = H]. Data for biol. activity of I were given.

IT **40878-10-2P**, 3-Cyano-3-(3,4-dichlorophenyl)-pentanedioic acid diethyl ester

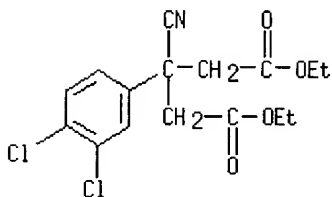
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**

(**Preparation**); RACT (Reactant or reagent)

(prepn. of 4-aryl-1-[2-(1-benzoyl-3-pyrrolidinyl)ethyl]piperidine-4-carboxamides as NK1 and NK2 receptor antagonists)

RN **40878-10-2** HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
 (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 6 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 1998:689192 HCAPLUS

DOCUMENT NUMBER: 129:330656

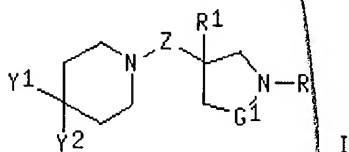
TITLE: Preparation of 1-(3-pyrrolidinylalkyl)-4-piperidinecarboxamides as tachykinin antagonists

INVENTOR(S): Burkholder, Timothy P.; Kudlacz, Elizabeth M.; Le

PATENT ASSIGNEE(S): Tieu-bihn; Maynard, George D.  
 SOURCE: Hoechst Marion Roussel Inc., USA  
 U.S., 93 pp., Cont.-in-part of U.S. 5,635,510.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 3  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5824690	A	19981020	US 1997-798664	19970211
ZA 9403091	A	19950112	ZA 1994-3091	19940504
US 5635510	A	19970603	US 1994-332027	19941031
PRIORITY APPLN. INFO.:			US 1993-58606	B2 19930506
			US 1994-225371	B2 19940419
			US 1994-332027	A2 19941031

OTHER SOURCE(S): MARPAT 129:330656  
 GI

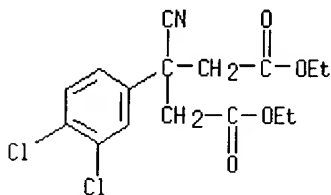


AB Title compds. [I; R = G<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>R<sub>2</sub>; G<sub>1</sub>, G<sub>2</sub> = CH<sub>2</sub> or CO; R<sub>1</sub> = (un)substituted Ph, -naphthyl, pyridyl, etc.; R<sub>2</sub> = (un)substituted Ph or -pyridyl; Y<sub>1</sub> = CONHR<sub>5</sub> or CONR<sub>6</sub>R<sub>7</sub>; R<sub>5</sub> = H, alkyl, (CH<sub>2</sub>)<sub>q</sub>NR<sub>6</sub>R<sub>7</sub>, etc.; R<sub>6</sub>, R<sub>7</sub> = alkyl; NR<sub>6</sub>R<sub>7</sub> = heterocyclyl; Y<sub>2</sub> = (un)substituted phenyl(methyl), -pyridyl, -thienyl; Y<sub>1</sub>Y<sub>2</sub> = atoms to complete a ring; Z = (CH<sub>2</sub>)<sub>2-3</sub>; n = 0 or 1; q = 2 or 3] were prep'd. Thus, 3,4-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>CN was biscondensed with BrCH<sub>2</sub>CO<sub>2</sub>Et and the reduced product cyclized to give, after redn. and N-benzoylation, 1-benzoyl-3-(2-hydroxyethyl)-3-(3,4-dichlorophenyl)pyrrolidine. The latter was treated with MeSO<sub>2</sub>Cl and the product aminated by 4-phenylpiperidine-4-carboxamide (prepn. given) to give I (G<sub>1</sub> = CH<sub>2</sub>, R = Bz, R<sub>1</sub> = C<sub>6</sub>H<sub>3</sub>Cl<sub>2</sub>-3,4, Y<sub>1</sub> = CONH<sub>2</sub>, Y<sub>2</sub> = Ph, Z = CH<sub>2</sub>CH<sub>2</sub>). Data for biol. activity of I were given.

IT 40878-10-2P, Diethyl 3-cyano-3-(3,4-dichlorophenyl)pentanedioate  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. of 1-(3-pyrrolidinylalkyl)-4-piperidinecarboxamides as tachykinin antagonists)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
 (CA INDEX NAME)



103(9)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

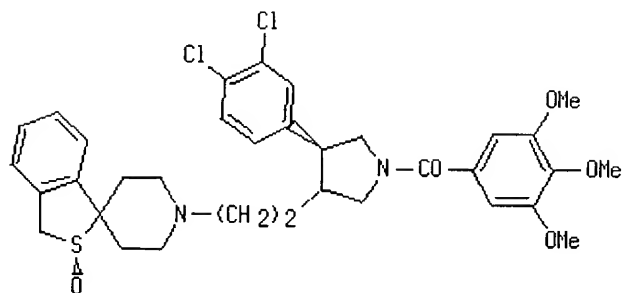
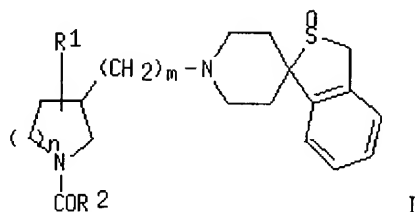
L24 ANSWER 7 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1998:665875 HCAPLUS  
 DOCUMENT NUMBER: 129:343481  
 TITLE: Preparation of N-(pyrrolidinylalkyl)spiro[benzo[c]thio  
 phene-1(3H),4'-piperidine] S-oxide derivatives as  
 substance P and neurokinin A receptor antagonists  
 INVENTOR(S): Nishi, Takehide; Fukazawa, Tetsuya; Yamaguchi,  
 Takeshi; Ito, kazuhiko; Ishibashi, Kimisige; Tamura,  
 Masakazu  
 PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan  
 SOURCE: Jpn. Kokai Tokkyo Koho, 24 pp.  
 CODEN: JKXXAF  
 DOCUMENT TYPE: Patent  
 LANGUAGE: Japanese  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 10273489	A2	19981013	JP 1998-13860	19980127
PRIORITY APPLN. INFO.:			JP 1997-18079	19970131
OTHER SOURCE(S):		MARPAT 129:343481		

GI



AB The title compds. [I; R1 = halophenyl; R2 = lower (halo)alkyl- or (halo)alkoxyphenyl; m, n = 1-3] are prepd. and specific compds. I are claimed. Also claimed are (1) antagonists of neurokinin 1 (NK1) and neurokinin 2 (NK2) receptor, (2) preventives or remedies for diseases mediated by tachykinin, and (3) preventives or remedies for asthma, bronchitis, rhinitis, allergy, and pollakiuria, contg. the compds. I as the reactive ingredients. Thus, spiro[benzo[c]thiophene-1(3H),4'-piperidin]-(2S)-oxide hydrochloride (prepn. given), 2-[(3S)-(3,4-dichlorophenyl)-1-(3,4,5-trimethoxybenzoyl)pyrrolidin-3-yl]ethyl methanesulfonate (prepn. given), NaHCO<sub>3</sub>, and KI were suspended in DMF and heated with stirring at 80° for 8 h to give the title compd. (II). II in vitro showed IC<sub>50</sub> of 5.1 ng/mL for inhibiting the binding of

[3H]substance P to NK1 receptor prepn. from Hartley guinea pig's lung air way and IC50 of 5.8 ng/mL for inhibiting the binding of [3H]-SR-48968 to NK2 receptor prepn. from Hartley guinea pig's ileum. A tablet and a capsule formulation contg. II were described.

IT 40878-10-2P

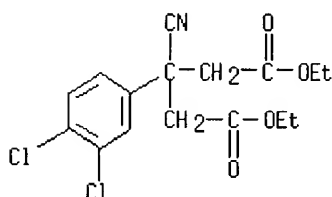
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**

(**Preparation**); RACT (Reactant or reagent)

(prepn. of N-(pyrrolidinylalkyl)spiro[benzo[c]thiophene-piperidine] S-oxide derivs. as substance P and neurokinin A receptor antagonists for drugs)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



L24 ANSWER 8 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 1998:424245 HCAPLUS  
DOCUMENT NUMBER: 129:95498  
TITLE: Novel heterocyclic carboxy-substituted cyclic carboxamide derivatives useful as tachykinin receptor antagonists  
INVENTOR(S): Burkholder, Timothy P.; Maynard, George D.; Kudlacz, Elisabeth M.  
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA  
SOURCE: PCT Int. Appl., 214 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>WO 9827085</u>	A1	19980625	<u>WO 1997-US21586</u>	19971121
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
<u>US 5977139</u>	A	19991102	<u>US 1997-971891</u>	19971117
<u>AU 9853627</u>	A1	19980715	<u>AU 1998-53627</u>	19971121
<u>AU 718984</u>	B2	20000504		
<u>EP 946545</u>	A1	19991006	<u>EP 1997-950690</u>	19971121
<u>EP 946545</u>	B1	20010905		
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
<u>CN 1240443</u>	A	20000105	<u>CN 1997-180774</u>	19971121

CN 1098259	B	20030108		
BR 9714156	A	20000208	BR 1997-14156	19971121
NZ 335883	A	20010727	NZ 1997-335883	19971121
AT 205200	E	20010915	AT 1997-950690	19971121
ES 2162686	T3	20020101	ES 1997-950690	19971121
PT 946545	T	20020228	PT 1997-950690	19971121
JP 2002512596	T2	20020423	JP 1998-527720	19971121
RU 2199535	C2	20030227	RU 1999-115883	19971121
CA 2275602	C	20030722	CA 1997-2275602	19971121
EE 4117	B1	20030815	EE 1999-254	19971121
ZA 9711264	A	19980623	ZA 1997-11264	19971215
NO 9903012	A	19990818	NO 1999-3012	19990618
KR 2000057667	A	20000925	KR 1999-705495	19990618
HK 1020571	A1	20020517	HK 1999-105551	19991130
PRIORITY APPLN. INFO.:			US 1996-794157	A 19961219
			US 1997-971891	A 19971117
			WO 1997-US21586	W 19971121
OTHER SOURCE(S):		MARPAT 129:95498		
GI				

\* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT \*

AB The invention relates to novel carboxy-substituted cyclic carboxamide derivs. I and stereoisomers and pharmaceutically acceptable salts thereof [wherein either G1 or G2 = CH<sub>2</sub>, while other = CO; m = 2 or 3; n = 0 or 1; R1 = 1-3 of H, halo, CF<sub>3</sub>, alkyl, alkoxy; R2 = 1-3 of H, halo, cyano, CF<sub>3</sub>, alkyl, alkoxy; R3 = 1-tetrazolyl or its 5-alkyl or 5-CF<sub>3</sub> derivs., 1,2,4-triazol-4-yl, 1H-tetrazol-5-yl; Ar = (un)substituted Ph or pyridyl; A = carboxy- or carboxy-deriv.-substituted pyrrolidino, piperazino, morpholino, thiomorpholino or oxides, or piperidino]. As tachykinin receptor antagonists, the compds. are useful in the treatment of tachykinin-mediated diseases and conditions, including particularly asthma, cough, and bronchitis. For instance, (S)-3-(3,4,5-trimethoxybenzoyl)-3-(3,4-dichlorophenyl)-3-(2-methanesulfonyloxyethyl)pyrrolidine was condensed with 4-phenyl-4-[[[(S)-2-carbomethoxypyrrolidin-1-yl]carboxamidol]piperidine hydriodide to give title compd. II. The latter bound to NK1 and NK2 receptors in vitro with IC<sub>50</sub> values of 4.32 nM and 4.51 nM, resp.

IT 40878-10-2P

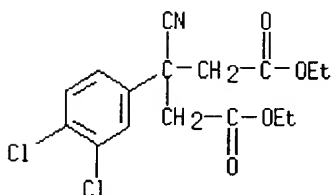
RL: RCT (Reactant); SPN (Synthetic preparation); PREP

(Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of heterocyclic carboxy-substituted cyclic carboxamide derivs. as tachykinin receptor antagonists)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



REFERENCE COUNT:

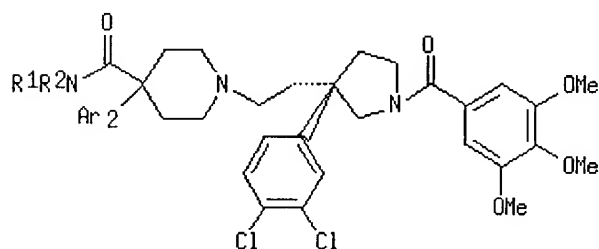
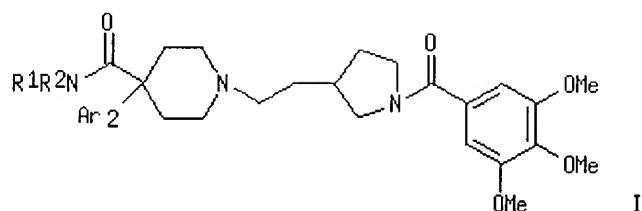
2

THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 9 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1997:723316 HCAPLUS  
 DOCUMENT NUMBER: 128:34664  
 TITLE: Synthesis and structure-activity relationships for a series of substituted pyrrolidine NK1/NK2 receptor antagonists  
 AUTHOR(S): Burkholder, Timothy P.; Kudlacz, Elizabeth M.; Maynard, George D.; Liu, Xiao-Gao; Le, Tieu-Binh; Webster, Mark E.; Horgan, Stephen W.; Wenstrup, David L.; Freund, David W.; Boyer, Fred; Bratton, Larry; Gross, Raymond S.; Knippenberg, Robert W.; Logan, Deborah E.; Jones, Bryan K.; Chen, Teng-Man; Geary, Julie L.; Correll, Melinda A.; Poole, J. Chuck; Mandagere, Arun K.; Thompson, Thomas N.; Hwang, Kin-Kai  
 CORPORATE SOURCE: Hoechst Marion Roussel, Cincinnati, OH, 45215, USA  
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1997), 7(19), 2531-2536  
 CODEN: BMCLE8; ISSN: 0960-894X  
 PUBLISHER: Elsevier  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 GI



AB The authors recently described the synthesis and characterization of MDL 105,212, a non peptide tachykinin antagonist with high affinity for NK1 and NK2 receptors. Here, the authors report the synthesis and structure-activity relationships for a series of analogs of MDL 105,212, I (Ar1 = 3-ClC6H4, 4-FC6H4, 3-pyridyl, etc., Ar2 = Ph, 3-MeOC6H4, 4-FC6H4, 3-, 4-pyridyl, R1R2N, = H2N, piperidino, morpholino, 4-methylpiperidino) and II (Ar2 = Ph, 3-, 4-pyridyl, R1R2N = H2N, morpholino, 4-methylpiperidino), with regards to NK1 and NK2 receptor binding affinity, phys.-chem. characterization; in vitro absorption potential; in vitro metabolic stability; and efficacy in a capsaicin-challenge conscious guinea pig model after oral administration.

IT 40878-10-2P

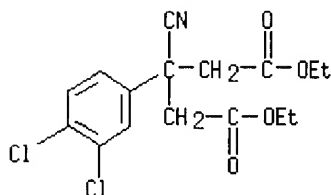
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP** (Preparation); RACT (Reactant or reagent)



(prepn. and structure activity relationship of pyrrolidines as neurokinin receptor antagonists)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 10 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 1997:618075 HCAPLUS  
DOCUMENT NUMBER: 127:278145  
TITLE: Preparation of 3-aryl-3-carboxyalkyl glutarimides  
INVENTOR(S): Camus, Philippe; Descamps, Marcel; Radisson, Joel  
PATENT ASSIGNEE(S): Sanofi, Fr.; Camus, Philippe; Descamps, Marcel; Radisson, Joel  
SOURCE: PCT Int. Appl., 41 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: French  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732852	A1	19970912	WO 1997-FR388	19970305
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
FR 2745811	A1	19970912	FR 1996-2880	19960307
FR 2745811	B1	19980522		
CA 2244771	AA	19970912	CA 1997-2244771	19970305
AU 9721634	A1	19970922	AU 1997-21634	19970305
EP 888304	A1	19990107	EP 1997-914357	19970305
EP 888304	B1	20011004		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 11506124	T2	19990602	JP 1997-531525	19970305
JP 3116051	B2	20001211		
BR 9707943	A	19990727	BR 1997-7943	19970305
AT 206399	E	20011015	AT 1997-914357	19970305
PT 888304	T	20020228	PT 1997-914357	19970305
ES 2165594	T3	20020316	ES 1997-914357	19970305
TW 381080	B	20000201	TW 1997-86102748	19970306
ZA 9701999	A	19970909	ZA 1997-1999	19970307

US 6008360	A	19991228	US 1998-142306	19980903
NO 9804083	A	19980904	NO 1998-4083	19980904
US 6242607	B1	20010605	US 1999-437362	19991110

PRIORITY APPLN. INFO.:

FR 1996-2880	A	19960307
WO 1997-FR388	W	19970305
US 1998-142306	A3	19980903

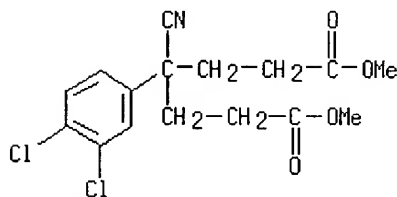
OTHER SOURCE(S): MARPAT 127:278145

AB RCR1R2ZCO2H [I; R = (un)substituted Ph, pyridyl, thienyl; R1R2 = CH2CH2CONHCO; Z = CH2 or CH2CH2] were prepd. by cyclization of I (R1 = cyano, R2 = CH2CH2CN or CH2CH2CO2H).

IT **65619-22-9P**, Dimethyl 4-cyano-4-(3,4-dichlorophenyl)heptanedioate  
 RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); **PREP (Preparation)**; RACT (Reactant or reagent)  
 (prepn. of 3-aryl-3-carboxyalkyl glutarimides)

RN 65619-22-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI)  
 (CA INDEX NAME)



103 (aw)

L24 ANSWER 11 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1997:501538 HCAPLUS

DOCUMENT NUMBER: 127:135815

TITLE: Novel substituted 4-(1H-benzimidazol-2-yl)-[1,4]-diazepanes useful for the treatment of allergic diseases

INVENTOR(S): Kane, John M.; Maynard, George D.; Burkholder, Timothy P.; Bratton, Larry D.; Dalton, Christopher R.; Santiago, Braulio; Kudlacz, Elizabeth M.

PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA

SOURCE: PCT Int. Appl., 349 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

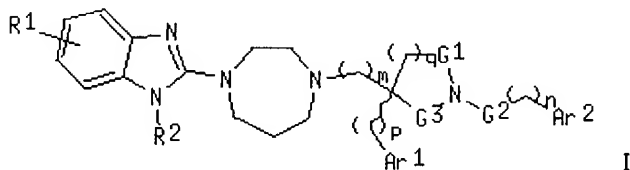
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9722604	A1	19970626	WO 1996-US19524	19961204
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2241827	AA	19970626	CA 1996-2241827	19961204
CA 2241827	C	20020430		
AU 9714119	A1	19970714	AU 1997-14119	19961204

AU 707914	B2	19990722		
EP 874843	A1	19981104	EP 1996-944267	19961204
EP 874843	B1	20020807		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1207097	A	19990203	CN 1996-199141	19961204
CN 1080262	B	20020306		
BR 9612074	A	19990330	BR 1996-12074	19961204
JP 2000500772	T2	20000125	JP 1997-522863	19961204
NZ 325581	A	20000327	NZ 1996-325581	19961204
AT 221883	E	20020815	AT 1996-944267	19961204
ES 2177827	T3	20021216	ES 1996-944267	19961204
PT 874843	T	20021231	PT 1996-944267	19961204
ZA 9610602	A	19970620	ZA 1996-10602	19961217
NO 9802867	A	19980819	NO 1998-2867	19980619
HK 1017684	A1	20021025	HK 1999-102816	19990705

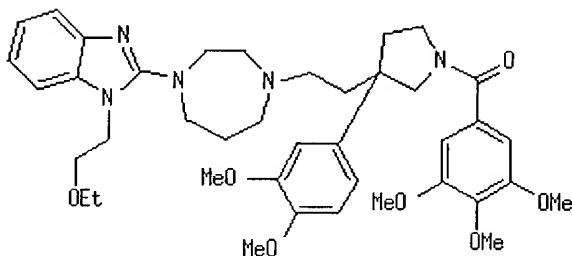
## PRIORITY APPLN. INFO.:

US 1995-580004	A	19951220
US 1996-736411	A	19961024
WO 1996-US19524	W	19961204

OTHER SOURCE(S): MARPAT 127:135815  
GI



I



II

AB The invention relates to novel 4-(1H-benzimidazol-2-yl)-[1,4]-diazepane derivs. I and their stereoisomers and pharmaceutically acceptable salts, which are useful as histamine receptor antagonists and tachykinin receptor antagonists (no data) [wherein m = 2, 3; n = 0, 1; q = 1, 2; p = 0, 1; G1 = CH2, CO; G2 = CH2, CHMe, CO; G3 = CH2, CO; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl; Ar2 = (un)substituted Ph, 3,4-methylenedioxy- or 3,4-ethylenedioxyphenyl; R1 = H, halo, CF3, alkyl, alkoxy; R2 = H, certain (un)substituted alkyl or alkenyl, etc.]. Such antagonists are useful in the treatment of allergic rhinitis, including seasonal rhinitis and sinusitis, inflammatory bowel diseases, including Crohn's disease and ulcerative colitis, asthma, bronchitis, and emesis. Over 90 synthetic examples are given. For instance, 3-(3,4-dimethoxyphenyl)-3-(2-hydroxyethyl)pyrrolidine (prepn. given) underwent a sequence of amidation with 3,4,5-trimethoxybenzoyl chloride, conversion to the mesylate ester, and condensation of the mesylate with the corresponding diazepane deriv., to give title compd. II.

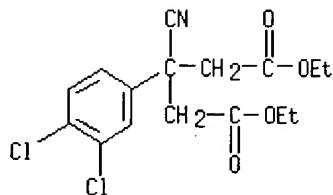
## IT 40878-10-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of benzimidazolyl diazepanes as antiallergics and antiinflammatories)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



L24 ANSWER 12 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full  
Text

Citing  
References

ACCESSION NUMBER: 1997:453985 HCAPLUS  
DOCUMENT NUMBER: 127:81450  
TITLE: Substituted 4-(1H-benzimidazol-2-ylamino)piperidines  
useful for the treatment of allergic diseases  
INVENTOR(S): Kane, John M.; Maynard, George D.; Burkholder, Timothy  
P.; Bratton, Larry D.; Dalton, Christopher R.;  
Santiago, Braulio; Kudlacz, Elizabeth M.  
PATENT ASSIGNEE(S): Hoechst Marion Roussel, Inc., USA  
SOURCE: PCT Int. Appl., 323 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 5  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9719074	A1	19970529	WO 1996-US18001	19961107
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
JP 2000500742	T2	20000125	JP 1997-517638	19961030
CA 2237971	AA	19970529	CA 1996-2237971	19961107
CA 2237971	C	20020122		
AU 9710508	A1	19970611	AU 1997-10508	19961107
AU 703701	B2	19990401		
CN 1202894	A	19981223	CN 1996-198360	19961107
CN 1098264	B	20030108		
EP 920425	A1	19990609	EP 1996-941334	19961107
EP 920425	B1	20030219		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 11513991	T2	19991130	JP 1997-519767	19961107
IL 124396	A1	20010319	IL 1996-124396	19961107
AT 232858	E	20030315	AT 1996-941334	19961107
ES 2188801	T3	20030701	ES 1996-941334	19961107
PT 920425	T	20030731	PT 1996-941334	19961107

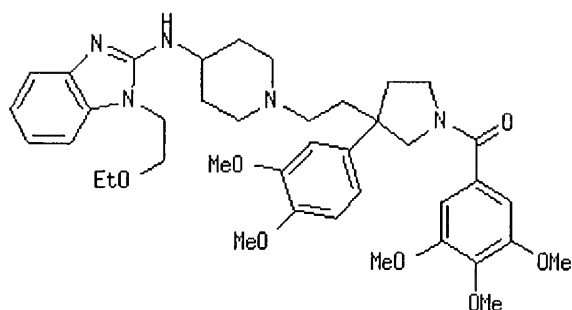
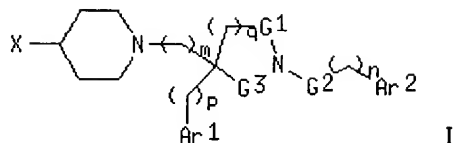
<u>ZA 9609484</u>	A	19970610	<u>ZA 1996-9484</u>	19961112
<u>TW 394771</u>	B	20000621	<u>TW 1996-85115760</u>	19961220
<u>NO 9802238</u>	A	19980701	<u>NO 1998-2238</u>	19980515
<u>HK 1018065</u>	A1	20030606	<u>HK 1999-103106</u>	19990720

PRIORITY APPLN. INFO.:

<u>US 1995-560419</u>	A	19951117
<u>US 1996-734508</u>	A	19961017
<u>US 1995-8108P</u>	P	19951030
<u>US 1995-7473P</u>	P	19951122
<u>US 1995-8992P</u>	P	19951221
<u>US 1996-13747P</u>	P	19960320
<u>US 1996-13748P</u>	P	19960320
<u>US 1996-13764P</u>	P	19960320
<u>US 1996-17455P</u>	P	19960517
<u>US 1996-17892P</u>	P	19960517
<u>US 1996-22047P</u>	P	19960722
<u>US 1996-23494P</u>	P	19960907
<u>WO 1996-US18001</u>	W	19961107

OTHER SOURCE(S):                    MARPAT 127:81450

GI



AB The invention relates to novel substituted piperidine derivs. I [ $m = 2, 3$ ;  $n = 0, 1$ ;  $q = 1, 2$ ;  $p = 0, 1$ ;  $G1 = CH_2, CO$ ;  $G2 = CH_2, CHMe, CO$ ;  $G3 = CH_2, CO$ ;  $Ar1 =$  (un)substituted Ph, naphthyl, pyridyl, or thienyl;  $Ar2 =$  (un)substituted Ph, benzodioxol-5-yl, benzodioxan-6-yl;  $X =$  (un)substituted benzimidazol-2-ylamino; with several provisos] and their stereoisomers and pharmaceutically acceptable salts. The compds. are useful as histamine receptor antagonists and tachykinin receptor antagonists (no data). Such antagonists are useful in the treatment of allergic rhinitis, including seasonal rhinitis and sinusitis, inflammatory bowel diseases, including Crohn's disease and ulcerative colitis, asthma, bronchitis, and emesis. For example, 3-(3,4-dimethoxyphenyl)-3-(2-hydroxyethyl)pyrrolidine (prepn. given) underwent amidation with 3,4,5-trimethoxybenzoyl chloride, followed by mesylation with  $MeSO_2Cl$  and  $Et_3N$ , and coupling with [1-(2-ethoxyethyl)-1H-benzimidazol-2-yl](piperidin-4-yl)amine (prepn. given), to give title compd. II.

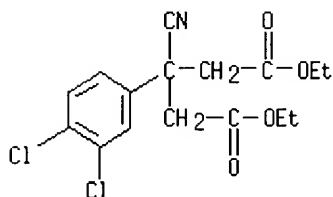
IT 40878-10-2P

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**  
(Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of (benzimidazolylamino)piperidines as  
antiallergics)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



L24 ANSWER 13 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full  
Text

Citing  
References

ACCESSION NUMBER: 1997:375289 HCAPLUS

DOCUMENT NUMBER: 127:95200

TITLE: Substituted pyrrolidin-3-yl-alkyl-piperidines useful  
as tachykinin antagonists

INVENTOR(S): Burkholder, Timothy P.; Kudlacz, Elizabeth M.;  
Maynard, George D.

PATENT ASSIGNEE(S): Merrell Pharmaceuticals Inc., USA

SOURCE: U.S., 82 pp., Cont.-in-part of U.S. Ser. No. 225,371,  
abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

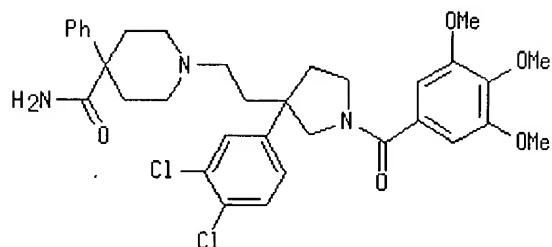
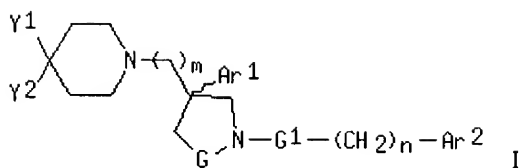
FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
<u>US 5635510</u>	A	19970603	<u>US 1994-332027</u>	19941031
<u>CN 1124961</u>	A	19960619	<u>CN 1994-192362</u>	19940422
<u>CN 1081635</u>	B	20020327		
<u>ZA 9403091</u>	A	19950112	<u>ZA 1994-3091</u>	19940504
<u>US 5648366</u>	A	19970715	<u>US 1995-477167</u>	19950607
<u>US 5861416</u>	A	19990119	<u>US 1997-795576</u>	19970206
<u>US 5824690</u>	A	19981020	<u>US 1997-798664</u>	19970211
<u>PRIORITY APPLN. INFO.:</u>			<u>US 1993-58606</u>	B2 19930506
			<u>US 1994-225371</u>	B2 19940419
			<u>US 1994-332027</u>	A3 19941031

OTHER SOURCE(S): MARPAT 127:95200

GI



AB The invention relates to substituted pyrrolidinyl-3-yl-alkyl-piperidines I [G, G1 = CH<sub>2</sub>, CO; m = 2, 3; n = 0, 1; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl, or benzo[1,3]dioxan-5-yl; Ar2 = (un)substituted Ph or pyridyl; Y1 = (un)substituted CONH<sub>2</sub>; Y2 = (un)substituted Ph, naphthyl, pyridyl, thienyl, or CH<sub>2</sub>Ph; or Y1Y2 = atoms to complete certain Ph-substituted, 5-membered, diazaspiro ring fusions], their stereoisomers, N-oxides, and pharmaceutically acceptable salts, and processes for prepn. of the same. I are useful for their pharmacol. activities, such as tachykinin antagonism, and esp. substance P and neurokinin A antagonism. Such compds. are indicated for conditions assocd. with neurogenic inflammation and other diseases. For instance, 3-(3,4-dichlorophenyl)-3-(2-hydroxyethyl)pyrrolidine underwent a sequence of amidation with 3,4,5-trimethoxybenzoyl chloride (71%), conversion of the alc. to a methanesulfonate ester (92%), and reaction of the mesylate moiety with 4-phenylpiperidine-4-carboxamide-HCl (71%), to give title compd. II. In an assay for modulation of NKA-induced respiratory effects in guinea pigs, II at 10 mg/kg reduced dyspnea to 60% of control.

IT **40878-10-2P**

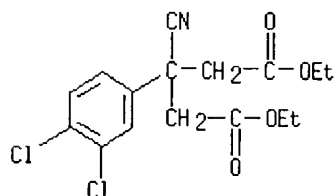
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**

(**Preparation**); RACT (Reactant or reagent)

(intermediate; prepn. of pyrrolidinylalkylpiperidines as tachykinin antagonists)

RN **40878-10-2** HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



L24 ANSWER 14 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full  
Text

Citing  
References

ACCESSION NUMBER:

1997:302959 HCAPLUS

DOCUMENT NUMBER:

126:277403

TITLE:

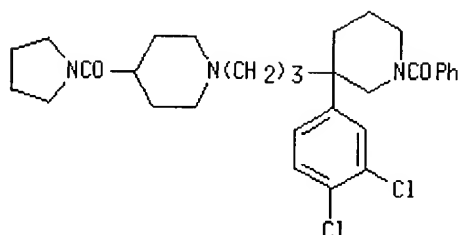
Novel human NK3 receptor-selective antagonist  
compounds containing them

INVENTOR(S): Bichon, Daniel; Edmonds-Alt, Xavier; Gueule, Patrick;  
 Proietto, Vincenzo; Van Broeck, Didier  
 PATENT ASSIGNEE(S): Sanofi, Fr.; Bichon, Daniel; Edmonds-Alt, Xavier;  
 Gueule, Patrick; Proietto, Vincenzo; Van Broeck,  
 Didier  
 SOURCE: PCT Int. Appl., 189 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9710211	A1	19970320	WO 1996-FR1416	19960913
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG				
FR 2738819	A1	19970321	FR 1995-10776	19950914
FR 2738819	B1	19971205		
CA 2232007	AA	19970320	CA 1996-2232007	19960913
AU 9669925	A1	19970401	AU 1996-69925	19960913
BR 9610081	A	19990105	BR 1996-10081	19960913
JP 11514983	T2	19991221	JP 1997-511718	19960913
EP 1019373	A1	20000719	EP 1996-931126	19960913
EP 1019373	B1	20031112		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
EP 1241168	A1	20020918	EP 2002-10824	19960913
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
AT 254104	E	20031115	AT 1996-931126	19960913
US 6028082	A	20000222	US 1998-43247	19980312
US 6291672	B1	20010918	US 1999-437203	19991109
US 2002049329	A1	20020425	US 2001-954862	20010918
US 6710042	B2	20040323		

PRIORITY APPLN. INFO.:  
 FR 1995-10776 A 19950914  
 EP 1996-931126 A3 19960913  
 WO 1996-FR1416 W 19960913  
 US 1998-43247 A3 19980312

OTHER SOURCE(S): MARPAT 126:277403  
 GI



AB Piperidinopropylpiperidine derivs. were prepd. for use as human NK3 receptor antagonists (no data). Thus, 3,4-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>CN was treated with



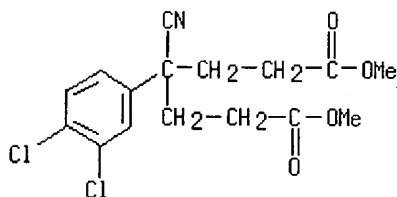
CH<sub>2</sub>:CHCO<sub>2</sub>Me to give 3,4-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>CH(CN)(CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>Me)<sub>2</sub> which was cyclized to the piperidonepropanoate and reduced to 3-(3,4-dichlorophenyl)-3-(3-hydroxypropyl)piperidine (I). I was N-benzoylated, converted to the mesylate, and aminated to give the piperidinopropylpiperidine II.

IT 65619-22-9P

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**  
(Preparation); RACT (Reactant or reagent)  
(prepn. of piperidinopropylpiperidines as NK3 antagonists)

RN 65619-22-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI)  
(CA INDEX NAME)



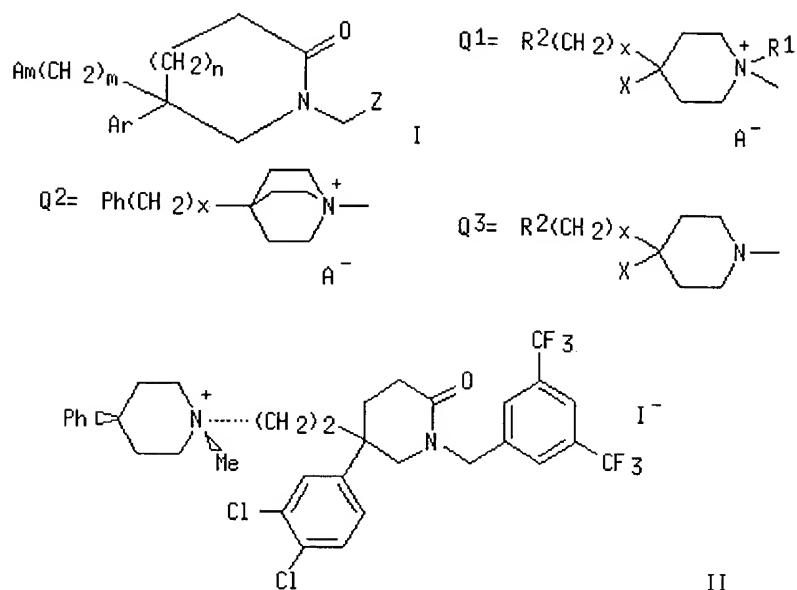
L24 ANSWER 15 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full  
Text

Citing  
References

ACCESSION NUMBER: 1996:544033 HCAPLUS  
DOCUMENT NUMBER: 125:195439  
TITLE: Heterocyclic compounds as tachykinin receptor antagonists, process for their preparation, and pharmaceuticals containing them  
INVENTOR(S): Emonds-Alt, Xavier; Grossriether, Isabelle; Proietto, Vincenzo; Van Broeck, Didier  
PATENT ASSIGNEE(S): Sanofi, Fr.  
SOURCE: Eur. Pat. Appl., 23 pp.  
CODEN: EPXXDW  
DOCUMENT TYPE: Patent  
LANGUAGE: French  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 723959	A1	19960731	EP 1996-400202	19960129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2729951	A1	19960802	FR 1995-1015	19950130
FR 2729951	B1	19970418		
EP 1101757	A1	20010523	EP 2001-100819	19960129
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV				
JP 08245622	A2	19960924	JP 1996-14703	19960130
US 5656639	A	19970812	US 1996-593929	19960130
US 5859029	A	19990112	US 1997-787910	19970123
PRIORITY APPLN. INFO.:			FR 1995-1015	A 19950130
			EP 1996-400202	A3 19960129
			US 1996-593929	A3 19960130
OTHER SOURCE(S):		MARPAT 125:195439		
GI				



AB Title compds. I [ $m = 2, 3$ ;  $n = 0, 1, 2$ ;  $\text{Am}$  = piperidinium group Q1, quinuclidinium group Q2, and (when  $n = 0$ ) piperidine group Q3;  $\text{R1}$  = alkyl, benzyl;  $\text{R2}$  = (un)substituted Ph;  $\text{X} = \text{H}, \text{OH}$ ;  $x = 0, 1$ ;  $\text{Ar}$  = (halo)phenyl, naphthyl, indolyl;  $\text{Z} = \text{Ph}$  optionally substituted by halo, alkyl, or  $\text{CF}_3$ ;  $\text{A}^-$  = anion] and their acid salts and solvates are claimed. The compds. have a strong affinity for NK1 receptors, and are useful for treatment of substance P-mediated pathologies, such as pain, allergy, inflammation, etc. For example, 4-phenylpiperidine was N-alkylated by 5-[2-(methoxy)ethyl]-5-(3,4-dichlorophenyl)-1-[3,5-bis(trifluoromethyl)benzyl]piperid-2-one [prepn. given], followed by quaternization with MeI to give the axial-Me-isomeric title compd. II, plus its equatorial-Me isomer. In a test for inhibition of substance P binding at human lymphoblastic receptors, II had a  $K_i$  on the order of  $0.1 \times 10^{-9}$  M, whereas a similar known compd. from EP-0512901 had  $K_i$  of only approx.  $10^{-6}$  M.

IT **40878-10-2P**, Diethyl 3-cyano-3-(3,4-dichlorophenyl)-1,5-pentanedioate

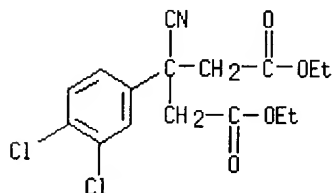
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**

(Preparation); RACT (Reactant or reagent)

(intermediate; prepn. of quinuclidinium and piperidine derivs. as tachykinin receptor antagonists)

RN **40878-10-2** HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



L24 ANSWER 16 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

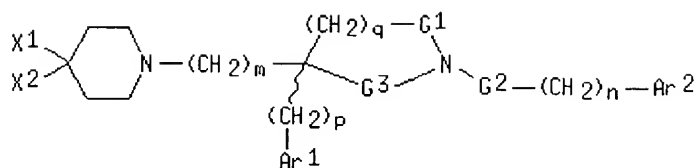
ACCESSION NUMBER:

1996:404635 HCAPLUS

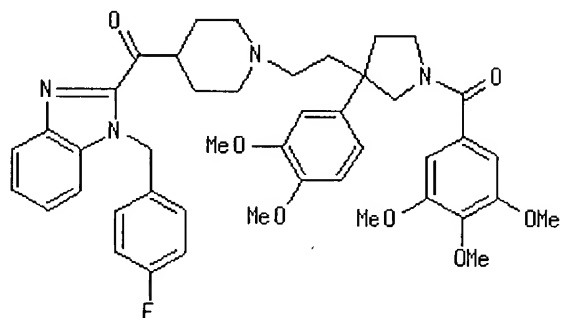
DOCUMENT NUMBER: 125:114615  
 TITLE: 1-Benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivatives and analogs as histamine and tachykinin receptor antagonists useful for the treatment of allergic diseases  
 INVENTOR(S): Burkholder, Timothy P.; Bratton, Larry D.; Kudlacz, Elizabeth M.; Maynard, George D.; Kane, John M.; Santiago, Braulio  
 PATENT ASSIGNEE(S): Merrell Dow Pharmaceuticals Inc., USA  
 SOURCE: PCT Int. Appl., 294 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9606094	A1	19960229	WO 1995-US10640	19950817
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2198084	AA	19960229	CA 1995-2198084	19950817
AU 9534928	A1	19960314	AU 1995-34928	19950817
AU 693936	B2	19980709		
EP 777666	A1	19970611	EP 1995-931551	19950817
EP 777666	B1	19990303		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1158612	A	19970903	CN 1995-195283	19950817
CN 1067385	B	20010620		
HU 76644	A2	19971028	HU 1997-1257	19950817
HU 221434	B	20021028		
JP 10504580	T2	19980506	JP 1995-508257	19950817
AT 177095	E	19990315	AT 1995-931551	19950817
ES 2132709	T3	19990816	ES 1995-931551	19950817
ZA 9507033	A	19960416	ZA 1995-7033	19950822
IL 115040	A1	20000229	IL 1995-115040	19950823
TW 430663	B	20010421	TW 1995-84108797	19950823
FI 9700771	A	19970224	FI 1997-771	19970224
NO 9700831	A	19970418	NO 1997-831	19970224
PRIORITY APPLN. INFO.:				
			US 1994-295960	A 19940825
			US 1995-501914	A 19950713
			WO 1995-US10640	W 19950817

OTHER SOURCE(S): MARPAT 125:114615  
 GI



I



II

AB The present invention relates to novel substituted piperidine derivs. I wherein: G1 is CH2 or CO; G2 is CH2 or CO; G3 is CH2 or CO; m is 2 or 3; n is 0 or 1; q is 1 or 2; p is 0 or 1; Ar1 = (un)substituted Ph, naphthyl, pyridyl, thienyl; Ar2 = (un)substituted Ph, pyridyl; X1 and X2 are defined in one of (A), (B), or (C): (A) X1 = H and X2 = substituted benzothiazole-2-carbonyl, diphenylmethyl, benzimidazolyl-2-carbonyl; (B) X1 = OH and X2 = substituted benzothiazol-2-yl, benzimidazol-2-yl; (C) X2 = (R5C6H4)C(Z1)(C6H4R6) wherein R5, R6 = from 1 to 3 substituents chosen independently from, e.g., H, halo, CF3, and X1 and Z1 taken together form a second bond between the carbon atoms bearing X1 and Z1; provided that when G1 is CO, then G2 and G3 are CH2, and that when G2 is CO, then G1 and G3 are CH2, and that when G3 is CO, then G1 and G2 are CH2; stereoisomers thereof, and pharmaceutically acceptable salts thereof which are useful as histamine receptor antagonists and tachykinin receptor antagonists. Such antagonists are useful in the treatment of allergic diseases including: seasonal rhinitis, allergic rhinitis, and sinusitis. Thus, e.g., substitution reaction of 4-[1-(4-fluorobenzyl)-1H-benzimidazole-2-carbonyl]piperidine with 1-(3,4,5-trimethoxybenzoyl)-3-(3,4-dimethoxyphenyl)-3-(2-methanesulfonyloxyethyl)pyrrolidine (prepn. given) afforded II which exhibited H1 receptor antagonism in vitro with pA2 = 7.50, and NK1 receptor binding affinity with IC50 = 31 nM.

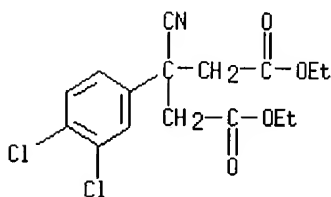
IT 40878-10-2P

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP** (Preparation); RACT (Reactant or reagent)

(1-benzoyl-3-[2-[4-(1H-benzimidazole-2-carbonyl)piperidin-1-yl]ethyl]-3-phenylpyrrolidine derivs. and analogs as histamine and tachykinin receptor antagonists useful for the treatment of allergic diseases)

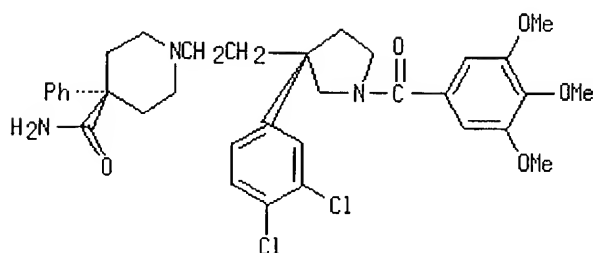
RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



Full Text	Citing References
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ACCESSION NUMBER: 1996:288884 HCAPLUS  
DOCUMENT NUMBER: 125:33442  
TITLE: Identification and chemical synthesis of MDL 105,212, a non-peptide tachykinin antagonist with high affinity for NK1 and NK2 receptors  
AUTHOR(S): Burkholder, Timothy P.; Kudlacz, Elizabeth M.; Le, Tieu-Binh; Knippenberg, Robert W.; Shatzer, Scott A.; Maynard, George D.; Webster, Mark E.; Horgan, Stephen W.  
CORPORATE SOURCE: Hoechst Marion Roussel, Cincinnati, OH, 45215, USA  
SOURCE: Bioorganic & Medicinal Chemistry Letters (1996), 6(8), 951-956  
CODEN: BMCLE8; ISSN: 0960-894X  
PUBLISHER: Elsevier  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI



I

103 (A)

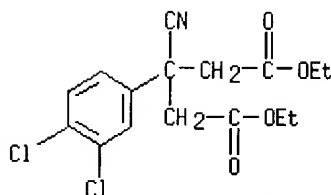
AB A nonpeptide tachykinin receptor antagonist 105,212 (I) was identified that has high affinity for human NK1 (IC<sub>50</sub> = 3.11 nM) and NK2 (IC<sub>50</sub> = 8.40 nM) receptors. The chem. synthesis of MDL 105212 and the structure-activity relationship of a series of racemic amide analogs are described.

IT 40878-10-2P

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP** (Preparation); RACT (Reactant or reagent)  
(prepn. of MDL 105212 non-peptide tachykinin antagonist)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



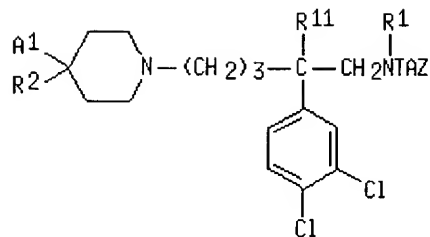
L24 ANSWER 18 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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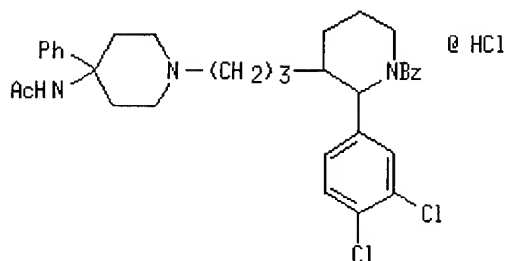
ACCESSION NUMBER: 1995:994586 HCAPLUS  
DOCUMENT NUMBER: 124:117093  
TITLE: Preparation of N-[(3,4-dichlorophenyl)propyl]piperidine selective human NK3-receptor antagonists

INVENTOR(S) : Bichon, Daniel; Van, Broeck Didier; Proietto, Vincenzo; Gueule, Patrick; Emonds-Alt, Xavier  
 PATENT ASSIGNEE(S) : SANOFI, Fr.  
 SOURCE: Eur. Pat. Appl., 61 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: French  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 673928	A1	19950927	EP 1995-400590	19950317
EP 673928	B1	20010829		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
FR 2717477	A1	19950922	FR 1994-3193	19940318
FR 2717477	B1	19960607		
FR 2717478	A1	19950922	FR 1994-9478	19940729
FR 2717478	B1	19960621		
FR 2719311	A1	19951103	FR 1995-571	19950119
FR 2719311	B1	19980626		
PL 185075	B1	20030228	PL 1995-307723	19950316
FI 9501265	A	19950919	FI 1995-1265	19950317
NO 9501044	A	19950919	NO 1995-1044	19950317
AU 9514909	A1	19950928	AU 1995-14909	19950317
AU 693845	B2	19980709		
ZA 9502228	A	19951221	ZA 1995-2228	19950317
HU 72065	A2	19960328	HU 1995-806	19950317
CN 1128756	A	19960814	CN 1995-103542	19950317
CN 1056605	B	20000920		
IL 113026	A1	19990620	IL 1995-113026	19950317
RU 2143425	C1	19991227	RU 1995-103737	19950317
AT 204863	E	20010915	AT 1995-400590	19950317
PT 673928	T	20020228	PT 1995-400590	19950317
ES 2164746	T3	20020301	ES 1995-400590	19950317
TW 380138	B	20000121	TW 1995-84102614	19950318
CA 2145000	AA	19950919	CA 1995-2145000	19950320
CA 2145000	C	20020507		
JP 08048669	A2	19960220	JP 1995-61419	19950320
JP 2922816	B2	19990726		
US 5741910	A	19980421	US 1996-607976	19960229
US 5942523	A	19990824	US 1996-608718	19960229
NO 9705089	A	19950919	NO 1997-5089	19971104
HK 1005137	A1	20020315	HK 1998-104342	19980519
US 6124316	A	20000926	US 1999-306825	19990507
US 6294537	B1	20010925	US 1999-306821	19990507
PRIORITY APPLN. INFO.:				
			FR 1994-3193	A 19940318
			FR 1994-9478	A 19940729
			FR 1995-571	A 19950119
			US 1995-405833	A3 19950317
			US 1997-880832	B1 19970623
OTHER SOURCE(S) : MARPAT 124:117093				
GI				



I



II

AB The title compds. [I; A = direct bond, CH<sub>2</sub>, CH<sub>2</sub>CH<sub>2</sub>, CH:CH; A1 = (un)substituted 2-pyridyl or Ph; R1 = Me; R2 = HO, alkoxy, CN, (un)substituted NH<sub>2</sub>, etc.; R11 = H; such that R1R11 = (CH<sub>2</sub>)<sub>3</sub>] (e.g., II; m.p. 184°), useful as human NK<sub>3</sub>-receptor antagonists (no data) for the treatment of neurokinin B-induced diseases (no data), are prepd.

IT **65619-22-9P**

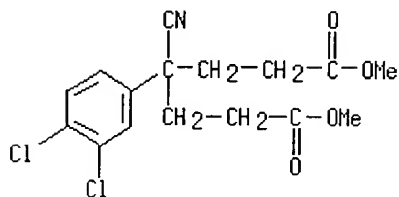
RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**

(**Preparation**); RACT (Reactant or reagent)

(prepn. of N-[(3,4-dichlorophenyl)propyl]piperidine selective human NK<sub>3</sub>-receptor antagonists from)

RN **65619-22-9** HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI)  
(CA INDEX NAME)



103(0)

L24 ANSWER 19 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER:

1995:772578 HCAPLUS

DOCUMENT NUMBER:

123:198629

TITLE:

Preparation of substituted (pyrrolidin-3-ylalkyl)piperidines as tachykinin antagonists

INVENTOR(S):

Burkholder, Timothy P.; Le, Tieu-Binh; Kudlacz, Elizabeth M.; Maynard, George D.

PATENT ASSIGNEE(S):

Merrell Dow Pharmaceuticals Inc., USA

SOURCE:

PCT Int. Appl., 238 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

PATENT NO.

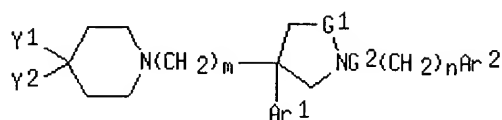
KIND DATE

APPLICATION NO. DATE

WO 9426735	A1	19941124	WO 1994-US4498	19940422
W: AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, KZ, LK, LU, LV, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, UZ, VN				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2160462	AA	19941124	CA 1994-2160462	19940422
CA 2160462	C	19981215		
AU 9469426	A1	19941212	AU 1994-69426	19940422
AU 678023	B2	19970515		
EP 696280	A1	19960214	EP 1994-917898	19940422
EP 696280	B1	19970924		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
HU 74085	A2	19961128	HU 1995-3153	19940422
JP 09500361	T2	19970114	JP 1994-525453	19940422
JP 3424174	B2	20030707		
AT 158580	E	19971015	AT 1994-917898	19940422
ES 2110761	T3	19980216	ES 1994-917898	19940422
IL 109496	A1	20000726	IL 1994-109496	19940502
ZA 9403091	A	19950112	ZA 1994-3091	19940504
FI 9505258	A	19951130	FI 1995-5258	19951102
NO 9504400	A	19960108	NO 1995-4400	19951103
PRIORITY APPLN. INFO.:			US 1993-58606	A 19930506
			US 1994-218483	A 19940328
			US 1994-225371	A 19940419
			WO 1994-US4498	W 19940422

OTHER SOURCE(S): MARPAT 123:198629

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AB Title compds. I (G1, G2 = CH<sub>2</sub>, CO; m = 2,3; n = 0,1; Ar<sub>1</sub>, Y<sub>2</sub> = (substituted)aryl, (substituted)heterocyclyl; Ar<sub>2</sub> = (substituted)Ph or heterocyclyl; Y<sub>1</sub> = (substituted)HNCO, (dialkylamino)carbonyl, N-heterocyclylcarbonyl; Y<sub>1</sub>Y<sub>2</sub> together with the C to which they are attached form a substituted spirocyclyl), or stereoisomers, or salts thereof, are prepd. I are claimed for treatment of neurogenic inflammatory diseases, asthma, pain, and cough. 3-(3,4-Dichlorophenyl)-3-(2-hydroxyethyl)pyrrolidine (prepn. given) was reacted with 2,4-dimethoxybenzoyl chloride to give 3-(3,4-dichlorophenyl)-1-(2,4-dimethoxybenzoyl)-3-(2-hydroxyethyl)pyrrolidine which in 2 steps was converted to I (G1 = H<sub>2</sub>C, G2 = CO, m = 2, n = 0, Ar<sub>1</sub> = 3,4-Cl<sub>2</sub>C<sub>6</sub>H<sub>3</sub>, Ar<sub>2</sub> = 2,4-(MeO)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>, Y<sub>1</sub> = H<sub>2</sub>NCO, Y<sub>2</sub> = Ph). Tachykinin antagonism was demonstrated.

IT 40878-10-2P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP

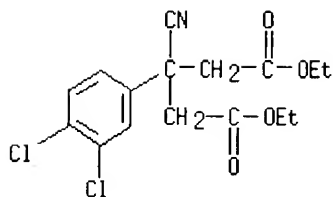
(Preparation); RACT (Reactant or reagent)

(prepn. of substituted (pyrrolidinylalkyl)piperidines as tachykinin antagonists)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)





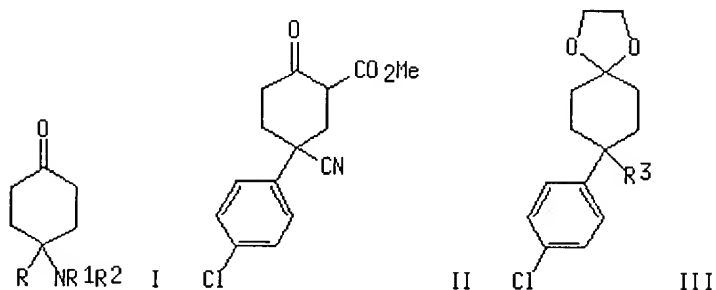
L24 ANSWER 20 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text	Citing References
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ACCESSION NUMBER: 1982:34690 HCAPLUS  
 DOCUMENT NUMBER: 96:34690  
 TITLE: 4-Amino-4-arylcyclohexanones and their ketals  
 INVENTOR(S): Lednicer, Daniel  
 PATENT ASSIGNEE(S): Upjohn Co. , USA  
 SOURCE: Can., 184 pp.  
 CODEN: CAXXA4  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 7  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 1100516	A2	19810505	CA 1980-352654	19800523
US 4065573	A	19771227	US 1976-692589	19760603
CA 1093553	A1	19810113	CA 1977-278494	19770516
IL 59312	A1	19840131	IL 1977-59312	19770520
US 4460604	A	19840717	US 1980-199415	19801022
PRIORITY APPLN. INFO.:			US 1976-692589	19760603
			CA 1977-278494	19770516
			IL 1977-52131	19770520
			US 1977-840861	19771011
			US 1979-23921	19790326

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AB Aminocyclohexanones I [R = thiopheno, (un)substituted Ph or arylalkoxy; R1 = C1-8 alkyl; R2 = C1-8 alkyl, C4-9 cycloalkylalkyl, C3-6 cycloalkyl, arylalkyl, aryloxyalkyl, alkoxy] (~230 compds.) were prepd. as analgesics (no data), e.g. from benzeneacetonitriles. Thus, adding 4-ClC6H4CH2CN to CH2:CHCO2Me in Me3COH gave (4-ClC6H4)(NC)C(CH2CH2CO2Me)2, which was cyclized with KOCMe3 to II whose decarboxylation and ketalization gave III (R3 = cyano). The last was hydrolyzed to the acid, converted into the isocyanate with Ph2P(O)N3, reduced with LiAlH4, and

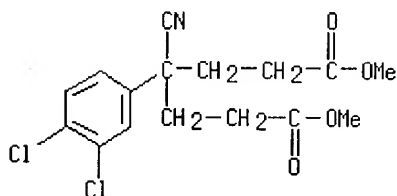
methylated with HCHO-NaBH<sub>4</sub> to give III (R<sub>3</sub> = NMe<sub>2</sub>).

IT **65619-22-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**  
(**Preparation**); RACT (Reactant or reagent)  
(prepn. and cyclization of)

RN 65619-22-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI)  
(CA INDEX NAME)



L24 ANSWER 21 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

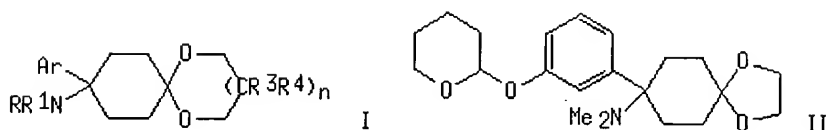
Full  
Text

Citing  
References

ACCESSION NUMBER: 1982:19734 HCAPLUS  
DOCUMENT NUMBER: 96:19734  
TITLE: 4-Amino-4-arylcyclohexanone ketals  
INVENTOR(S): Lednicer, Daniel  
PATENT ASSIGNEE(S): Upjohn Co. , USA  
SOURCE: Can., 185 pp. Division of Can. Appl. No. 278,494.  
CODEN: CAXXA4  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 7  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 1105938	A2	19810728	CA 1980-359623	19800905
US 4065573	A	19771227	US 1976-692589	19760603
CA 1093553	A1	19810113	CA 1977-278494	19770516
IL 59312	A1	19840131	IL 1977-59312	19770520
US 4460604	A	19840717	US 1980-199415	19801022
PRIORITY APPLN. INFO.:			US 1976-692589	19760603
			CA 1977-278494	19770516
			IL 1977-52131	19770520
			US 1977-840861	19771011
			US 1979-23921	19790326

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AB I [Ar = [(tetrahydro-2H-pyran-2-yl)oxylphenyl; R = C1-8 alkyl; R1 = C1-8 alkyl, C3-6 cycloalkyl [(C3-6-cycloalkyl)C1-3-alkyl], Rx2C6H5-xCH<sub>2</sub>, Rx2C6H5-xCH<sub>2</sub>CH<sub>2</sub>, Rx2C6H5-xOCH<sub>2</sub>CH<sub>2</sub> (R<sub>2</sub> = halo, CF<sub>3</sub>, C1-4 alkyl, C1-4 alkoxy; x = 0-2); n = 0 or 1; R<sub>3</sub> = H or Me; R<sub>4</sub> = H, Ph, alkenyl] were prepd. as analgesics (no data). Thus, 4-cyano-4-(dimethylamino)cyclohexanone cyclic ethylene ketal was treated with the

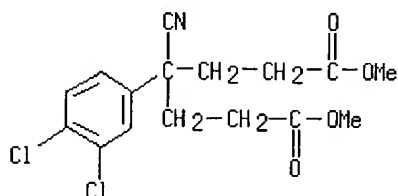
Grignard reagent from 2-(3-bromophenoxy)tetrahydro-2H-pyran to give II.

IT **65619-22-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**  
(Preparation); RACT (Reactant or reagent)  
(prepn. and cyclization of)

RN **65619-22-9** HCAPLUS

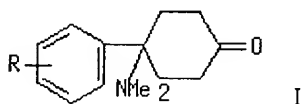
CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI)  
(CA INDEX NAME)



L24 ANSWER 22 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing  
References

ACCESSION NUMBER: 1980:180773 HCAPLUS  
DOCUMENT NUMBER: 92:180773  
TITLE: 4-Amino-4-arylcyclohexanones and their derivatives, a novel class of analgesics. 1. Modification of the aryl ring  
AUTHOR(S): Lednicer, Daniel; Von Voigtlander, Philip F.; Emmert, D. Edward  
CORPORATE SOURCE: Res. Lab., Upjohn Co., Kalamazoo, MI, 49001, USA  
SOURCE: Journal of Medicinal Chemistry (1980), 23(4), 424-30  
CODEN: JMCMAR; ISSN: 0022-2623  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
OTHER SOURCE(S): CASREACT 92:180773  
GI



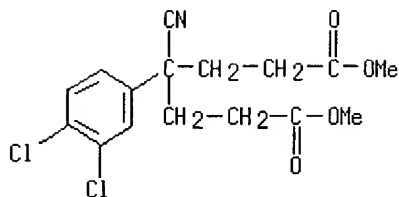
AB Synthesis of title compds. (I) involved double Michael reaction of Me acrylate with arylacetonitriles, followed by cyclization, decarboxylation, ketalization, and sapon.; the geminally substituted acid formed was rearranged to the isocyanate with (PhO)2PON3, and the isocyanates were converted into I via LiAlH4 redn. and methylation with CH2O. Analgesic activity was very sensitive to the nature and position of the substituent on the arom. ring. The most potent compds. in this series (I, R = 4-Me, 4-Br) showed 50% the potency of morphine. Deletion of the ring oxygen abolished activity.

IT **65619-22-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**  
(Preparation); RACT (Reactant or reagent)  
(prepn. and cyclization of)

RN **65619-22-9** HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI)  
(CA INDEX NAME)

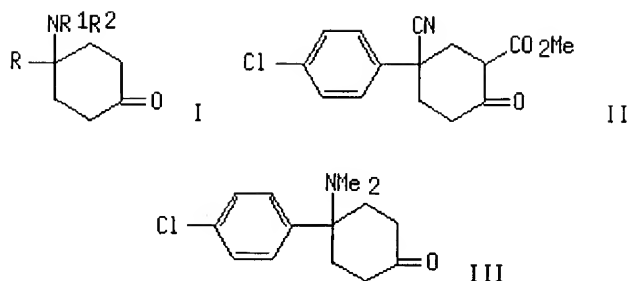


L24 ANSWER 23 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing  
References

ACCESSION NUMBER: 1978:104776 HCAPLUS  
DOCUMENT NUMBER: 88:104776  
TITLE: 4-Amino-4-arylcyclohexanone compounds and intermediates  
INVENTOR(S): Lednicer, Daniel  
PATENT ASSIGNEE(S): Upjohn Co., USA  
SOURCE: Ger. Offen., 273 pp.  
CODEN: GWXXBX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 7  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2723937	A1	19771215	DE 1977-2723937	19770526
US 4065573	A	19771227	US 1976-692589	19760603
ZA 7702819	A	19780726	ZA 1977-2819	19770511
IL 52131	A1	19840131	IL 1977-52131	19770520
IL 59312	A1	19840131	IL 1977-59312	19770520
AU 7725425	A1	19781130	AU 1977-25425	19770524
AU 511781	B2	19800904		
NL 7706051	A	19771206	NL 1977-6051	19770602
FR 2354992	A1	19780113	FR 1977-16901	19770602
ES 459429	A1	19781116	ES 1977-459429	19770602
GB 1561205	A	19800213	GB 1977-23366	19770602
GB 1561206	A	19800213	GB 1978-35783	19770602
BE 855405	A1	19771205	BE 1977-178211	19770603
JP 53018546	A2	19780220	JP 1977-65685	19770603
US 4180584	A	19791225	US 1977-840861	19771011
US 4460604	A	19840717	US 1980-199415	19801022
PRIORITY APPLN. INFO.:			US 1976-692589	19760603
			IL 1977-52131	19770520
			US 1977-840861	19771011
			US 1979-23921	19790326
OTHER SOURCE(S):		CASREACT 88:104776		
GI				



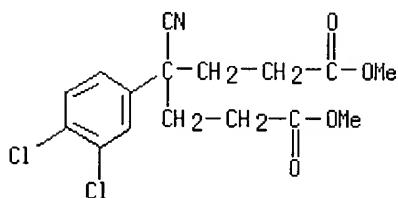
AB The title compds. (~200) I (R = thienyl, naphthyl, Ph, or substituted aryl; R1, R2 = Me, allyl, pentyl, Bu, etc.) and/or their cyclic ketals, useful as analgesics and narcotic antagonists, were prepd. Thus, 4-ClC6H4CH2CN with 2 mol. CH2:CHCO2Me followed by cyclization gave II, which on hydrolysis-decarboxylation, ketalization with HOCH2CH2OH, hydrolysis of the CN group to CO2H, conversion of the CO2H to isocyanato (by Ph3PN3), redn. of the isocyanate to NHMe, N-methylation, and hydrolysis of the ketal group gave III.

IT **65619-22-9P**

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP**  
(**Preparation**); RACT (Reactant or reagent)  
(prepn. and cyclization of)

RN 65619-22-9 HCAPLUS

CN Heptanedioic acid, 4-cyano-4-(3,4-dichlorophenyl)-, dimethyl ester (9CI)  
(CA INDEX NAME)



L24 ANSWER 24 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text    Citing  
References

ACCESSION NUMBER: 1974:146010 HCAPLUS  
DOCUMENT NUMBER: 80:146010  
TITLE: 1-Pyrrolidinylbutyrophenone derivatives  
INVENTOR(S): Bastian, Jean M.; Strasser, Michael  
PATENT ASSIGNEE(S): Sandoz Ltd.  
SOURCE: Ger. Offen., 65 pp.  
CODEN: GWXXBX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2345192	A1	19740328	DE 1973-2345192	19730907
NL 7312262	A	19740313	NL 1973-12262	19730906
US 3903111	A	19750902	US 1973-394685	19730906
GB 1440380	A	19760623	GB 1973-41914	19730906
BE 804701	A1	19740311	BE 1973-135531	19730910
JP 49069661	A2	19740705	JP 1973-101293	19730910
DD 108533	C	19740920	DD 1973-173381	19730910

AU 7360170	A1	19750313	AU 1973-60170	19730910
HU 167372	P	19750927	HU 1973-SA2530	19730910
ES 418619	A1	19760601	ES 1973-418619	19730910
AT 7307802	A	19770215	AT 1973-7802	19730910
SU 548206	D	19770225	SU 1973-1957934	19730910
FR 2198756	A1	19740405	FR 1973-32612	19730911
ZA 7307236	A	19750430	ZA 1973-7236	19730911
PRIORITY APPLN. INFO.:			CH 1972-13280	19720911
			CH 1972-16930	19721121

GI For diagram(s), see printed CA Issue.

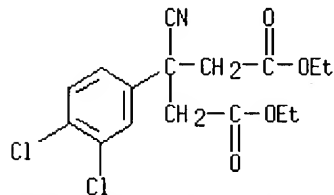
AB Analgesic pyrrolidinybutyrophenones I (R = Ph, substituted phenyl; R1 = H, Me, Et, Ac, COEt, COCMe3, CONHMe; n = 1, 2) and some related compds. (40 compds.) were prepd. Thus CH<sub>2</sub>(CO<sub>2</sub>Et)<sub>2</sub>, treated with PhCHO gave the PhCH:C(CO<sub>2</sub>Et)<sub>2</sub> which was treated with KCN in EtOH to give NCCHPhCH<sub>2</sub>CO<sub>2</sub>Et (II). Reaction of II with BrCH<sub>2</sub>CO<sub>2</sub>Et gave NCCPh(CH<sub>2</sub>CO<sub>2</sub>Et)<sub>2</sub> (III). Reductive cyclization of III gave Et 3-phenyl-5-oxopyrrolidine-3-acetate, which was successively hydrolyzed to the acid, reduced to the alc. with LiAlH<sub>4</sub> and treated with Cl(CH<sub>2</sub>)<sub>3</sub>COC<sub>6</sub>H<sub>4</sub>F-p to give I (R = Ph, R1 = H, n = 2).

IT 40878-10-2P

RL: RCT (Reactant); SPN (Synthetic preparation); **PREP** (Preparation); RACT (Reactant or reagent) (prepn. and reductive cyclization of)

RN 40878-10-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(3,4-dichlorophenyl)-, diethyl ester (9CI) (CA INDEX NAME)



L24 ANSWER 25 OF 25 HCAPLUS COPYRIGHT 2004 ACS on STN

Full Text Citing References

ACCESSION NUMBER: 1973:159422 HCAPLUS  
 DOCUMENT NUMBER: 78:159422  
 TITLE: Spiro heterocyclics  
 INVENTOR(S): Bastian, Jean Michel; Hasspacher, Klaus; Strasser, Michael  
 PATENT ASSIGNEE(S): Sandoz Ltd.  
 SOURCE: Ger. Offen., 44 pp.  
 CODEN: GWXXBX  
 DOCUMENT TYPE: Patent  
 LANGUAGE: German  
 FAMILY ACC. NUM. COUNT: 2  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2241027	A1	19730301	DE 1972-2241027	19720821
CH 556835	A	19741213	CH 1971-12318	19710823
ES 406008	A1	19760601	ES 1972-406008	19720421
SE 385584	B	19760712	SE 1972-10502	19720814
NL 7211304	A	19730227	NL 1972-11304	19720818
FR 2150797	A1	19730413	FR 1972-29540	19720818

BE 787804	A1	19730221	BE 1972-121173	19720821
PL 79446	P	19750630	PL 1972-157376	19720821
GB 1401048	A	19750723	GB 1972-38802	19720821
GB 1401049	A	19750723	GB 1975-4517	19720821
JP 48029765	A2	19730419	JP 1972-84027	19720822
HU 165127	P	19740628	HU 1972-SA2388	19720822
AT 7207228	A	19750915	AT 1972-7228	19720822
AT 330167	B	19760625		
DD 102146	C	19731212	DD 1972-165200	19720823
AU 7245897	A1	19740228	AU 1972-45897	19720823
ZA 7205796	A	19740424	ZA 1972-5796	19720823
ZA 7400329	A	19740529	ZA 1974-329	19720823
US 3901916	A	19750826	US 1973-419670	19731128
AT 7406072	A	19750915	AT 1974-6072	19740724
PRIORITY APPLN. INFO.:			CH 1971-12318	19710823
			US 1972-282609	19720821
			AT 1972-7228	19720822
			CH 1972-17291	19721128

GI For diagram(s), see printed CA Issue.

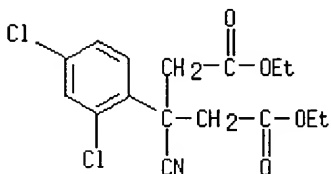
AB Analgesic spiro[indan-1,3'-pyrrolidin]yl-p-fluorobutyrophenones I (R = H, R1 = H, 6-MeO, 6-Cl, 4-Cl, 5-Cl, 4-MeO, 6-Me, 5-F, 5-MeO, 5-Me, 5-Me2CH, 5,7-Cl2, 5,7-Me2, 4,5-Cl2, 5,6-(MeO)2; R = Ac, MeNHCO, EtCO, R1 = H, 5-Cl, 5-Me) were prepd. Thus, PhCHO was treated with CH2-(CO2Et)2 to give PhCH:C(CO2Et)2, which with KCN gave PhCH(CN)CH2CO2Et. The latter was treated with BrCH2CO2Et to give PhC(CN)(CH2CO2Et)2, which was cyclized with Raney Ni to Et 5-oxo-3-phenyl-3-pyrrolidinylacetate. Hydrolysis of the ester to the free acid and cyclization with polyphosphoric acid gave spiro[indan-1,3'-pyrrolidine]-3,5'-dione. LiAlH4 redn. of the ketone yielded spiro[indan-1,3'-pyrrolidin]-3-ol, which on treatment with 2-(3-chloropropyl)-2-(p-fluorophenyl)-1,3-dioxolan or Cl(CH2)3COC6H4F-p gave I (R = R1 = H).

IT **40878-02-2P**

RL: SPN (Synthetic preparation); **PREP (Preparation)**  
(prepn. of)

RN 40878-02-2 HCAPLUS

CN Pentanedioic acid, 3-cyano-3-(2,4-dichlorophenyl)-, diethyl ester (9CI)  
(CA INDEX NAME)



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(FILE 'HOME' ENTERED AT 16:39:51 ON 16 MAY 2004)

FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004

L1 STRUCTURE UPLOADED

L2 0 S L1

L3 0 S L1 FULL

FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004

L4 STRUCTURE UPLOADED

L5 0 S L4

FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004

L6               STRUCTURE UPLOADED  
L7               0 S L6  
L8               0 S L6 FULL  
L9               STRUCTURE UPLOADED  
L10              3 S L9  
L11              48 S L9 FULL

FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004

L12              69 S L11  
L13              1 S L12 AND CASTRO, B?/AU  
L14              68 S L12 NOT L13  
L15              0 S L14 AND DORMOY, J?/AU  
L16              0 S L14 AND RABION, A?/AU

FILE 'REGISTRY' ENTERED AT 16:51:50 ON 16 MAY 2004

L17              STRUCTURE UPLOADED  
L18              0 S L17  
L19              9 S L17 FULL

FILE 'HCAPLUS' ENTERED AT 16:54:42 ON 16 MAY 2004

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L21              26 S L19/PREP  
L22              1 S L20 AND CASTRO, B?/AU  
L23              0 S L22 NOT L13  
L24              25 S L21 NOT L22

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L25              26 L19

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FULL ESTIMATED COST	135.47	774.10
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L26              0 L19



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FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004

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L3               0 S L1 FULL

FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004

L4               STRUCTURE UPLOADED  
L5               0 S L4

FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004

L6               STRUCTURE UPLOADED  
L7               0 S L6  
L8               0 S L6 FULL  
L9               STRUCTURE UPLOADED  
L10              3 S L9  
L11              48 S L9 FULL

FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004

L12              69 S L11  
L13              1 S L12 AND CASTRO, B?/AU  
L14              68 S L12 NOT L13  
L15              0 S L14 AND DORMOY, J?/AU  
L16              0 S L14 AND RABION, A?/AU

FILE 'REGISTRY' ENTERED AT 16:51:50 ON 16 MAY 2004

L17              STRUCTURE UPLOADED  
L18              0 S L17  
L19              9 S L17 FULL

FILE 'HCAPLUS' ENTERED AT 16:54:42 ON 16 MAY 2004

L20              26 S L19  
L21              26 S L19/PREP  
L22              1 S L20 AND CASTRO, B?/AU  
L23              0 S L22 NOT L13  
L24              25 S L21 NOT L22  
L25              26 S L19

FILE 'CAOLD' ENTERED AT 16:57:59 ON 16 MAY 2004

L26              0 S L19

=> file hcaplus

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	0.42	774.52
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-18.71

FILE 'HCAPLUS' ENTERED AT 16:58:29 ON 16 MAY 2004

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FILE COVERS 1907 - 16 May 2004 VOL 140 ISS 21  
FILE LAST UPDATED: 14 May 2004 (20040514/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his

(FILE 'HOME' ENTERED AT 16:39:51 ON 16 MAY 2004)

FILE 'REGISTRY' ENTERED AT 16:39:58 ON 16 MAY 2004

L1 STRUCTURE UPLOADED  
L2 0 S L1  
L3 0 S L1 FULL

FILE 'BEILSTEIN' ENTERED AT 16:44:35 ON 16 MAY 2004

L4 STRUCTURE UPLOADED  
L5 0 S L4

FILE 'REGISTRY' ENTERED AT 16:45:38 ON 16 MAY 2004

L6 STRUCTURE UPLOADED  
L7 0 S L6  
L8 0 S L6 FULL  
L9 STRUCTURE UPLOADED  
L10 3 S L9  
L11 48 S L9 FULL

FILE 'HCAPLUS' ENTERED AT 16:50:43 ON 16 MAY 2004

L12 69 S L11  
L13 1 S L12 AND CASTRO, B?/AU  
L14 68 S L12 NOT L13  
L15 0 S L14 AND DORMOY, J?/AU  
L16 0 S L14 AND RABION, A?/AU

FILE 'REGISTRY' ENTERED AT 16:51:50 ON 16 MAY 2004

L17 STRUCTURE UPLOADED  
L18 0 S L17  
L19 9 S L17 FULL

FILE 'HCAPLUS' ENTERED AT 16:54:42 ON 16 MAY 2004

L20 26 S L19  
L21 26 S L19/PREP  
L22 1 S L20 AND CASTRO, B?/AU  
L23 0 S L22 NOT L13  
L24 25 S L21 NOT L22  
L25 26 S L19

FILE 'CAOLD' ENTERED AT 16:57:59 ON 16 MAY 2004

L26 0 S L19

FILE 'HCAPLUS' ENTERED AT 16:58:29 ON 16 MAY 2004

```
=> s l11/thu
      69 L11
      592984 THU/RL
L27      0 L11/THU
          (L11 (L) THU/RL)
```

```
=> s l11/thu
      69 L11
      592984 THU/RL
L28      0 L11/THU
          (L11 (L) THU/RL)
```

```
=> s l11 not l19
      69 L11
      26 L19
L29      60 L11 NOT L19
```

```
=>
```